

Histopathology of the filum terminale in children with and without tethered cord syndrome with attention to the elastic tissue within the filum

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Abstract

Purpose To compare histologically transected fila from pediatric patients with tethered cord syndrome (TCS), with and without a low conus, with controls, focusing on collagenous and elastic tissue.

Methods Thirty fila from patients with TCS, including 5 where minimal cautery was used prior to filum section, were compared with fila from 27 pediatric cadavers without TCS (controls). Sections of fila were stained with H&E, Masson trichrome and Verhoeff von Gieson elastic stains, and 7 with Gordon and Sweet's reticulin stain.

Results Fila from controls showed loose fibrous connective tissue (FCT) with thin and evenly dispersed elastic fibers (EFs). Reticulin fibers (RFs) were seen in blood vessel walls and nerve twigs. Fat was identified microscopically in 2 fila.

All fila from patients with TCS had dense FCT. The EFs were in normal numbers in 17, and focally or diffusely decreased in 13. All 25 patients where the fila were cauterized during resection had thick and coiled EFs. Coiling was not seen when minimal cautery was applied. RFs were seen in blood vessel walls and nerve twigs. Fat was identified in 19 patients. Findings were similar, whether the conus termination was normal or low.

Conclusion The fila of all patients with TCS, whether or not the conus was low, showed abnormal FCT. EFs were decreased in 48 % of patients; however, there were thick and coiled EFs in all patients. Coiling of EFs, initially thought to be an abnormality in patients, is considered most likely to be a result of cautery (i.e., artifactual/iatrogenic coiling).

Keywords Occult tethered cord · Fibrous connective tissue · Reticulin · Cautery

Introduction

Tethered cord syndrome (TCS) is a clinical entity manifested by neurological, urological, and/or orthopedic dysfunction caused by tethering of and traction on the conus medullaris. Reduced filum elasticity is thought to exert traction on the conus, which may cause the clinical symptoms and signs of the syndrome [1]. In TCS associated with a tight filum, a low-lying conus medullaris is expected, with the tip of the conus located below the L2-L3 vertebral disc level [2].

More recently, an “occult tethered cord syndrome” (OTCS) has been described, wherein the conus is thought to be tethered by the filum, but the conus ends in a normal location. In this situation, the size and appearance of the filum may be normal [3–10], making it difficult to understand how the filum could be tethering the spinal cord. Some studies of the histopathology of the filum in OTCS have indicated that these fila contain excessive collagen and abnormal elastic tissue, which may reduce elasticity of the filum [11, 12]. The aim of this study was to examine histologically transected fila from pediatric patients with TCS with and without a low-lying conus and compare these fila to those from cadavers (normal controls), focusing on the collagen and elastic tissue.

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Materials and methods

Approval for the study was obtained from the Clinical Research Ethics Board of BC Children's Hospital and the University of British Columbia (H08-01919).

Children who had section of the filum for either classical TCS (conus abnormally low = Group 1) or OTCS (conus in normal position = Group 2) from 1983 to 2008 were identified from a prospectively maintained database in the Division of Neurosurgery. Those patients in whom a piece of filum had been examined histopathologically were included in this study. In these study patients, the standard operative procedure was to cauterize, with bipolar cautery, the upper and lower parts of the filum in the surgical field, then cut the filum at these two points and send the intermediate part of the filum to the pathologist. Fila from autopsied children aged 36 weeks gestational age to 16 years, with no neurological, urological, orthopedic, spinal, or cutaneous abnormality were taken prospectively, examined similarly, and considered as the control group. A 3–4-cm segment from the tip of the conus to the distal filum was cut out sharply without any cautery and examined histopathologically. All filum specimens were reviewed by two neuropathologists (GH and CD).

From our results we noted visible cautery coagulation with hematoxylin and eosin (H&E) stain in all the fila with TCS and OTCS. Thus, in a second phase of the study, additional fila were taken at surgery using minimal or no cautery prior to resecting the piece of filum for pathological examination (Group 3). For control purposes, the ends of one filum were cauterized following transection at autopsy (control case 27).

Fila were examined in cross and longitudinal section. Specimens were fixed in 10 % phosphate-buffered formalin for 24 h at room temperature, dehydrated through a series of graded alcohols (70, 95, and 100 %) for 1 h per station and then cleared in xylene for 1 h per station. The tissue was embedded in paraffin, sectioned at 4 microns, dewaxed in xylene for 10 min, and rehydrated through graded alcohols (100 and 95 %) for 1 min each. Sections were stained with H&E, Masson trichrome (MTr), and Verhoeff von Gieson (VVG) elastic stain, coverslipped and examined. Fila in which tissue was available for staining were stained with Gomori and Sweet's (G&S) reticulin stain.

Data collected on the clinical cases, included the following: patient's age, symptoms, level of conus termination, filum thickness (>2 mm was considered abnormal) [13], and presence of fat on MRI. On histopathological examination, data collected included the following: nature of fibrous tissue, fat, nerve fascicles, vascular tissue, ganglia, ependymal tissue, glial tissue, and elastic fibers (EFs). The fibrous connective tissue (FCT) was assessed qualitatively with H&E and MTr stains and scored as loose, moderately dense, and dense. In "loose FCT," individual collagen fibers were separate and easily discernible. In "moderately dense FCT," there was separation

between collagen fibers with compact areas. In "dense FCT," there was minimal to no separation between the collagen fibers. The EFs were assessed qualitatively with VVG stain in terms of distribution, thickness, and alteration in appearance. The distribution of RFs was assessed with G&S stain.

Results

Seventy-five children had filum section for either TCS or OTCS between 1983 and 2008. Of these, 25 fila were removed using the standard technique of bipolar cautery prior to cutting the filum. Another five patients had fila sectioned with minimal or no cautery. There were 27 controls.

In the 27 controls (Table 1), there were nerve fascicles in 26, ganglia in 14, glial tissue in all 27 (particularly in the proximal third of the filum), and microscopic foci of fat in 2. Ependymal canals or a central canal was seen in the proximal third and in 17, the ependyma tapered caudally to form a strand of ependymal cells which extended to the periphery and surface of the filum. The vessels of the filum were dilated, medium-sized veins and small arteries/veins. With H&E and MTr stains the fibrous tissue was loose in 19 controls, while it was loose with focal moderately dense areas in 8. There were no controls where the FCT was dense or moderately dense throughout. With VVG stain, the EFs were evenly distributed in all controls, with thin EFs in 23 and slightly thicker in 4. There was no coiling of EF in any of the controls. In the filum (case 27) where cautery was applied to a cadaver filum, the EFs were thin, evenly distributed in the tissue, and there was no coiling.

In the initial 25 patients (standard bipolar cautery used), the conus was low on MRI in 10 (TCS—Table 2, group 1) and normally located in 15 (OTCS—Table 3, group 2). On MRI, the filum was abnormally thick in 14 and fat was identified in 6 patients.

Histologically, H&E stain showed fat in 19, and in 7 (5/10 TCS and 2/15 OTCS) the resected filum was composed predominantly of fat. Glial tissue was present in 5, nerves in 25, ependyma in 2, and ganglion cells in 2 patients. Small arteries/veins were present and the veins were dilated in 11.

There was dense FCT in all 25 fila with TCS and OTCS with H&E and MTr stains. In one patient with OTCS, there was also loose FCT. No patient had loose FCT throughout, as was typical in controls. With VVG stain, the EFs were in normal numbers in 13, focally decreased in 11, and diffusely decreased in 1 patient. There were thick and thin EFs in 16 and only thick fibers in the remaining 9 patients.

In all 25 patient fila, cautery coagulation was seen with H&E staining; this was at both ends of the specimen in 4 (Fig. 1), at one end in 6, focally in 6, and throughout the entire specimen in 9. With VVG stain, in the areas of cautery, there were thickened and coiled EFs (Fig. 2a). There was 100 % correlation between coiling and thickening of the EFs and

Table 1 Controls: fila from cadavers with no neurological, urological, orthopedic, or spinal cutaneous abnormality

Case	Age	Fibrous tissue	Nerves (Y/N)	Adipose tissue (Y/N)	Vascular tissue	Ganglia (Y/N)	Ependymal tissue	Glial tissue (Y/N)	Masson trichrome stain	Elastic stain
1	8 years	Loose with focal mod dense FCT	Y	N	Mod sized vein, small veins and arteries	Y	Central canal prox	Y	Loose with focal mod dense FCT	Thin, evenly dispersed fibers
2	8 years	Loose FCT	Y	N	Mod sized and small veins	N	Central canal prox, ependymal canals distally	Y	Loose FCT	Thin, evenly dispersed fibers
3	36 weeks GA	Loose FCT	Y	Y Very small amount	Dilated capillaries	N	Central canal prox	Y	Loose FCT	Thin, evenly dispersed fibers
4	17 months	Loose FCT	Y	N	Dilated capillaries	N	Central canal prox, ependymal canals distally	Y	Loose FCT	Thin, evenly dispersed fibers
5	9 years	Loose FCT	Y	N	Mod sized dilated veins and small arteries	N	Central canal prox, ependymal canals and ependymal cells distally	Y	Loose FCT	Slightly thicker fibers, evenly dispersed
6	2 months	Loose FCT	Y	N	Mod sized dilated veins and small arteries	Y	Central canal prox, ependymal canals distally	Y	Loose FCT	Thin, evenly dispersed fibers
7	7 months	Loose FCT	Y	N	Mod sized dilated veins and small arteries	N	Central canal prox	Y	Loose FCT	Thin, evenly dispersed fibers
8	2 months	Loose FCT	Y	N	Dilated veins	N	Central canal prox, ependymal canals distally	Y	Loose FCT	Slightly thicker fibers, evenly dispersed
9	39 weeks GA	Loose FCT	N	N	Dilated veins and capillaries	N	Central canal prox, ependymal canals distally	Y	Loose FCT	Thin with some thicker fibers, evenly dispersed
10 ^b	3 months	Loose FCT	Y	N	Mod sized dilated veins and small arteries	Y	Central canal prox, ependymal canals and ependymal cells distally	Y	Loose FCT	Thin, evenly dispersed fibers
11	40 weeks GA	Loose FCT	Y	N	Mod sized dilated veins	Y	Central canal prox, ependymal cells distally	Y	Loose FCT	Thin, evenly dispersed fiber
12 ^b	8 months	Loose with focal mod dense FCT	Y	Y Very small amount	Non dilated veins	N	Central canal prox, ependymal canals and ependymal cells distally	Y, with spheroids	Loose with focal mod dense FCT	Thin, evenly dispersed fibers
13	16 years	Loose FCT	Y	N	Dilated veins, arteries and capillaries	N	Central canal prox, ependymal cells extend on surface distally	Y	Loose FCT	Thin, evenly dispersed fibers
14	7 years	Loose with focal mod dense FCT	Y	N	Mod sized vein, small veins and arteries	N	Central canal prox	Y	Loose with focal mod dense FCT	Thin, evenly dispersed fibers
15 ^b	40 weeks GA	Loose FCT	Y	N	Dilated veins and less prominent small arteries	Y	Central canal prox, ependymal canals and ependymal cells distally on surface	Y	Loose FCT	Thin, evenly dispersed fibers, a few thicker fibers
16 ^b	12 years	Loose FCT	Y	N	Dilated veins and focally dilated arteries	N	Central canal prox, ependymal canals and ependymal cells distally on surface	Y	Loose FCT	Thin, evenly dispersed fibers
17	17 days	Loose FCT	Y	N	Non dilated veins	Y	Central canal prox, ependymal canals distally	Y	Loose FCT	Thin, evenly dispersed fibers

Table 1 (continued)

Case	Age	Fibrous tissue	Nerves (Y/N)	Adipose tissue (Y/N)	Vascular tissue	Ganglia (Y/N)	Ependymal tissue	Glial tissue (Y/N)	Masson trichrome stain	Elastic stain
18	6 months	Loose with focal mod dense FCT	Y	N	Dilated veins and a few arteries	Y	Central canal prox, ependymal canals and ependymal cells distally on surface	Y	Loose with focal mod dense FCT	Thin, evenly dispersed fibers, a few thicker fibers
19	5 months	Loose with focal mod dense FCT	Y	N	Mod sized and small veins	Y	Central canal prox, ependymal canals and ependymal cells distally on surface	Y	Loose with focal mod dense FCT	Thin, evenly dispersed fibers
20	1 months	Loose with focal mod dense FCT	Y	N	Mod sized and small veins	Y	Central canal prox, ependymal canals and ependymal cells distally on surface	Y	Loose with focal mod dense FCT	Thin, evenly dispersed fibers
21	39 weeks GA	Loose FCT	Y	N	Mod sized dilated veins and small arteries	Y	Central canal prox, ependymal canals and ependymal cells distally on surface	Y	Loose FCT	Thin, evenly dispersed fibers
22	3 years	Loose with focal mod dense FCT	Y	N	Mod sized dilated veins and small arteries	N	Central canal prox, ependymal canals and ependymal cells distally on surface	Y, with spheroids	Loose with focal mod dense FCT	Thin, evenly dispersed fibers
23	11 months	Loose FCT	Y	N	Mod sized dilated veins	Y	Central canal prox, ependymal canals and ependymal cells distally on surface	Y	Loose FCT	Thin, evenly dispersed fibers
24	1 months	Loose FCT	Y	N	Mod sized dilated veins	Y	Central canal prox, ependymal canals and ependymal cells distally on surface	Y	Loose FCT	Slightly thicker fibers, evenly dispersed
25	1 years	Loose FCT	Y	N	Dilated vein and arteries	Y	Central canal prox, ependymal canals and ependymal cells distally on surface	Y	Loose FCT	Slightly thicker fibers, evenly dispersed
26	6 years	Loose FCT	Y	N	Congested veins	Y	Central canal prox, ependymal canals and ependymal cells distally on surface	Y	Loose FCT	Thin, evenly dispersed fibers
27 ^a	3 months	Loose with focal mod dense FCT	Y	N	Congested veins	N	Ependymal canals prox and ependymal cells distally	Y	Loose with focal mod dense FCT	Thin, evenly dispersed fibers

GA gestational age, Y yes, N no, FCT fibrous connective tissue, mod moderately, prox proximally.

^a Cauterized filum

^b Filum stained with Gordon and Sweet's reticulin stain

Table 2 Group 1: fila resected from patients with TCS and with abnormally low termination of the conus

Case	Age	Symptoms and other abnormalities	Level of conus on MRI	Filum thick on MRI (Y/N)	Fat on MRI (Y/N)	H&E	Fat on histology	Masson trichrome stain	Elastic stain
1	1 year 7 months	Bowel incontinence Syrinx	L5–S1	Y	Y	Dense FCT, fat, nerves, dilated medium sized veins	Y Filum is predominantly fat	Dense FCT	Normal numbers. Thicker and coiled fibers associated with cautery
2	11 months	No symptoms Syrinx Vacterl	L3–4	Y	Y	Dense FCT, nerves, ganglion	Y Small amount	Dense FCT	Normal numbers. Thin, and focally thick and coiled fibers associated with cautery
3	3 months	No symptoms Syrinx Vacterl	L4	Y	N	Dense FCT, fat, nerves	Y Filum is predominantly fat	Dense FCT	Normal numbers. Thin and thick, coiled fibers associated with cautery
4	12 years	Left foot pain, mid back pain and scoliosis; split cord	L5	Y	N	Dense FCT, glial tissue, nerves, dilated veins, cartilage	N	Dense FCT	Normal numbers, thin, thick and coiled fibers associated with cautery
5	1 years 1 months	No symptoms Syrinx Vacterl	L4	Y	Y	Dense FCT, fat, nerves	Y Filum is predominantly fat	Dense FCT	Focally decreased. Some thin, but mostly thick and coiled fibers associated with cautery
6	7 months	No symptoms; cloacal extrophy	L3–4	Y	Y	Mainly fat, small amount of dense FCT, nerves	Y Filum is predominantly fat	Dense FCT	Normal numbers. Thick and coiled fibers associated with cautery
7	9 years 4 months	Urinary incontinence; split cord	L5–S1	Y	N	Dense FCT, nerves	N	Dense FCT	Focally decreased. Thin, thick and coiled fibers associated with cautery
8	9 years	No symptoms; cervical split cord	L5	Y	Y	Mainly fat, dense FCT, nerves, minimal glial tissue	Y Filum is predominantly fat	Dense FCT	Focally decreased. Thin, and mainly thick and coiled fibers associated with cautery
9	12 years 6 months	Size discrepancy R and L limbs; split cord	L3–4	Y	N	Dense FCT, glial tissue, nerve, dilated arteries and veins	N	Dense FCT	Normal numbers. Thin, but predominantly thick and coiled fibers associated with cautery
10	16 y 8 months	Back pain; split cord	L3–4	Y	N	Dense FCT, glial tissue, fat, nerves, dilated arteries and veins	Y	Dense FCT	Focally decreased. Thin, and mainly thick and coiled fibers associated with cautery

Y yes, N no, MRI magnetic resonance imaging, FCT fibrous connective tissue

Table 3 Group 2: fila resected from patients with TCS and with a normal position of conus

Case	Age	Symptoms and other abnormalities	Level of conus on MRI	Filum thick on MRI	Fat on MRI	H&E	Fat on histology (Y/N)	Masson trichrome stain	Elastic stain
1	9 years 8 months	Walking on heels more than toes	L1–2	N	N	Dense FCT, fat, nerves, few blood vessels	Y	Dense FCT	Focally decreased. Thin, and thick, coiled fibers associated with cautery
2	3 years 8 months	No symptoms Syrinx Vacterl	L1–2	N	N	Very dense FCT, nerve, few blood vessels	N	Dense FCT	Normal numbers. Evenly distributed thin, and thick, coiled fibers associated with cautery
3	15 years	Back pain, knee pain, inward turning of foot	L1–2	N	N	Dense FCT, fat, nerves, glial tissue, ependyma, dilated veins and arteries,	Y	Dense FCT	Focally decreased. Thin fibers except for area of cautery where fibers thicker and coiled
4	9 years 9 months	Incontinence	L1–2	N	N	Dense FCT, fat, nerves, blood vessels	Y	Dense FCT	Diffusely decreased. Thin and thick fibers. Scattered coiled fibers associated with cautery.
5	7 years 1 months	Nocturnal enuresis	L1–2	N	N	Dense FCT, ependyma, nerve, blood vessels	N	Dense FCT	Normal numbers. Thick and coiled fibers associated with cautery
6	5 years 11 months	Urinary tract infection, bladder and bowel incontinence	L2–3	N	N	Dense FCT, fat, nerves	Y	Dense FCT	Focally decreased. Thick and coiled fibers associated with cautery
7	8 years	Enuresis, encopresis, back pain and leg length discrepancy	L2–3	N	N	Dense FCT, fat, nerves, blood vessels	Y	Dense FCT	Numerous fibers but focally decreased. Thin fibers, several thick and coiled fibers associated with cautery
8	9 years 6 months	Enuresis	L1–2	N	N	Dense FCT, fat, nerves, arteries and dilated vein	Y	Dense FCT	Focally decreased. Thick and coiled fibers associated with cautery
9	9 years 8 months	Nocturnal enuresis, back pain Sacral dimple	L1	N	N	Dense FCT, fat, nerves, dilated veins	Y	Dense FCT	Normal numbers. A few thick, coiled fibers associated with cautery
10	10 years 7 months	Urinary tract infection	L2	N	N	Dense FCT, fat, nerves, dilated blood vessels	Y	Dense FCT	Focally decreased. Thin fibers but several thick and coiled fibers associated with cautery
11	6 years 10 months	Urinary incontinence	L1–2	N	N	Dense FCT, nerves, arteries, veins	N	Dense FCT	Normal numbers. Thick and coiled fibers associated with cautery
12	8 months	No symptoms; dermal pit	L1–2	Y	N	Dense FCT, nerves, ganglion, fat, dilated vein	Y	Dense FCT	Normal numbers. Fibers generally thin, with very focal thick, coiled fibers associated with cautery
13	7 years	Fecal incontinence	L2–3	Y	Y	Dense FCT, mainly fat, nerves, dilated arteries, veins	Y	Dense FCT	Normal numbers. Thick, coiled fibers particularly on periphery, associated with cautery
14	11 years 5 months	Minor weakness left ankle, itchy sensation in legs	L1–2	Y	N	Dense FCT, fat, nerves, dilated vein	Y	Dense FCT	Focally decreased, but still good numbers. Thick, coiled fibers associated with cautery
15	1 years 1 months	Decreased mobility lower and upper limbs	L2–3	Y	N	Dense FCT, fat, nerves, arteries, non-dilated veins	Y	Loose and dense FCT	Normal numbers. Thin, and thick, coiled fibers associated with cautery

Y yes, N no, MRI magnetic resonance imaging, FCT fibrous connective tissue

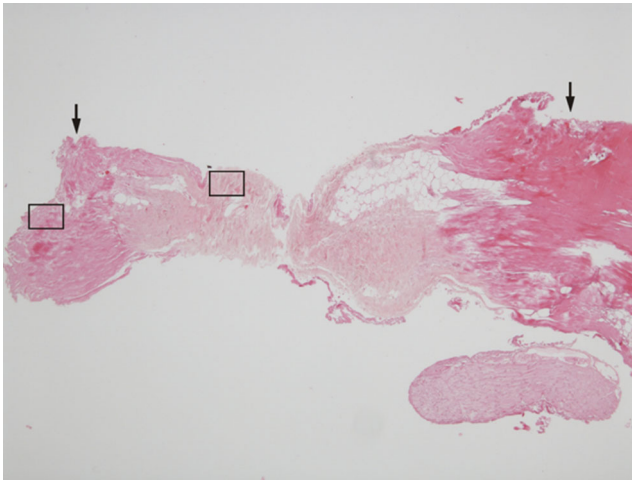


Fig. 1 **a** Filum with areas of cautery artifact (*arrows*) staining deeply eosinophilic (hematoxylin and eosin stain mag. $\times 50$). *Boxed area on left* corresponds to Fig. 2a. *Boxed area in center* corresponds to Fig. 2b

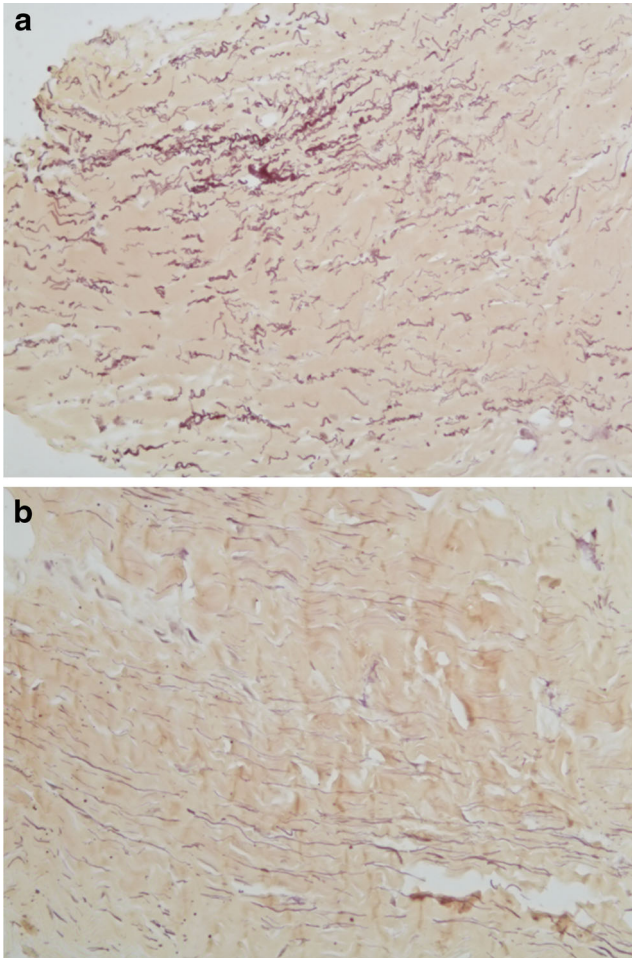


Fig. 2 **a** *Boxed area on left* in Fig. 1 showing thick and coiled elastic fibers in area of cautery coagulation (Verhoef von Gieson stain mag. $\times 400$). **b** *Central boxed area* in Fig. 1 with thin, non-coiled elastic fibers (Verhoef von Gieson stain mag. $\times 400$)

cautery coagulation. The EFs were thin and non-coiled in the non-cauterized areas (Fig. 2b).

In the five fila taken with minimal or no cautery (Table 4, group 3), there was dense FCT in all specimens. The five fila showed thin EFs; only one filum taken in the context of TCS having added thicker EFs. Only one of the five fila showed focal decrease in EFs. Coiled EFs were not seen in any of the five fila where minimal cautery was applied. The MRI and pathology findings are summarized in Table 5.

Four fila from the control group, and three from group 3, where minimal cautery was applied, were stained with G&S stain where tissue was available to determine more precisely what type of collagen comprised the dense FCT. All seven showed RFs within blood vessel walls and nerve twigs. There were no convincing RFs in the fibrous tissue in any of the fila.

Discussion

TCS secondary to a tight filum terminale is a well-recognized and clinically important problem in children and adults [3, 5, 14–16]. In OTCS [3–10, 17, 18], the symptoms are similar to classical TCS, but the conus is normal in position, with or without a thickened filum. In several studies, cutting the filum has resulted in postoperative improvement in urological function in over 70 % of patients [3–8, 10, 15, 19, 20].

The concept of tethering by the filum implies that the filum should be less elastic than normal and therefore should exert traction on the conus. It is easy to understand how an abnormally thick or fatty filum might be less elastic than normal and exert traction on the conus, which then lies in an abnormally low position. However, it is more difficult to conceptualize how a macroscopically normal filum would cause traction on the conus, especially when the conus ends in a normal position. One possibility is that the structure of the filum is different and is less elastic than normal, but perhaps not tight enough to result in an abnormally low conus.

Several studies have examined the histological and ultrastructural features of the normal filum [7, 21–25] and the filum in TCS with and without a low lying conus [7, 11, 12, 25, 26]. In these studies, the normal filum in the fetus and adult has fibrous tissue, nerve fascicles, ganglia, ependymal cells, glial tissue, and small blood vessels. In the studies by Tehli et al. and Kural et al., elastic fibers were not seen in the fetus [24, 25]. In addition, Kural et al. did not see type 1 collagen in the fetus, while type 3 collagen was observed around the perineurium of peripheral nerves and the walls of the filum vessels, leading them to conclude that the elasticity of the filum in intrauterine life is probably low [24]. Fontes et al. [22] demonstrated ultrastructurally in five adult cadavers that the bulk of the filum was composed of longitudinally oriented bundles of type 1 collagen fibers with transversal type 3 collagen fibers. Elaunin and elastic fibers were within the longitudinal

Table 4 Group 3: fila from patients with tethered cord syndrome and minimal caudery

Case	Age	Symptoms and other abnormalities	Level of conus on MRI	Filum thick on MRI (Y/N)	Fat on MRI (Y/N)	H&E	Fat on histology (Y/N)	Masson trichrome	Elastic
1 ^{a, b}	3 years	Decrease in right ankle reflex Split cord	L2-3	Y	Y	Dense FCT, glial tissue, ependymal canals, nerves, dorsal root ganglion	Y Minute amount	Dense FCT	Focally decreased. Thin fibers. No coiling
2 ^b	7 months	Urodynamic abnormalities Hydromyelia	L3	N	Y	Dense FCT, fat, nerves, glial tissue, ependyma, blood vessels	Y	Dense FCT	Thin and thicker fibers throughout. No coiling
3 ^b	4 months	Urodynamic abnormalities Imperforate anus, cleft lip and palate, horseshoe kidney, hydromyelia	L3	N	Y	Dense FCT, mainly fat, nerves, small veins	Y Filum is predominantly fat	Dense FCT	Thin fibers throughout. No coiling
4 ^a	9 years	Urodynamic abnormalities	L2	N	N	Dense FCT, nerves, small dilated veins	N	Dense FCT	Thin fibers throughout fibrous tissue. No coiling
5 ^a	13 years	Urinary tract infection, bladder and bowel incontinence Previous filum transection, Case 6 in group 1.	L2	N	N	Dense FCT, ependyma, small artery	N	Dense FCT	Thin fibers throughout. No coiling

Y yes, N no, FCT fibrous connective tissue

^a OTCS^b Filum stained with Gordon and Sweet's reticulin stain

fibers. The EM fiber composition did not differ significantly along the entire length of the filum terminale. In our study, the filum from the controls contained glial tissue, a central canal in the proximal filum that caudally tapered to ependymal canals and then a strand of ependymal cells on the periphery of the filum, nerves, and ganglion cells. FCT in the filum was loose or loose and moderately dense. Dense FCT was not seen in any of the control fila. EFs were seen in all control fila including the five fetuses in our study. The EFs were evenly distributed and thin in 23 and slightly thicker in 4 controls. The findings were similar throughout the filum. In two of the controls, there was a microscopic amount of adipose tissue. Kural et al [24] also found "adipocyte clusters" in 2 of their 15 controls, aged 15 and 25 weeks gestational age. Hence, its presence is likely abnormal, especially when found in histologic abundance or when seen on MRI.

In all studies examining the FCT in the filum with TCS, there was increase in FCT or dense FCT [7, 11, 20, 25, 26]. In this study, the FCT was abnormally dense in all 30 patients in groups 1, 2, and 3; only 1 patient with low-lying conus had loose FCT in addition to dense FCT. In none of the fila from patients with TCS was there loose FCT only. There was no difference in FCT in patients with normal position versus low-lying conus.

Regarding EFs, Barutcuoglu et al. found tissue hyalinization with disappearance of EFs in 33 patients with split cord malformation [11]. Yamada et al. [1] noted reduced elastin in 58 fila from patients with TCS. Ultrastructurally, Liu et al. showed sparse or invisible elastic and reticular fibers in the fila of patients with TCS, but these fibers were still visible in the relatively normal areas of the fila. In our study, when we looked at the patients in whom the fila had been removed in the standard fashion with the use of bipolar cautery above and below the resected specimen, the number of EFs was focally decreased in 11/25 patients and diffusely decreased in 1 patient. The EFs were thin and thick in 16/25 patients and purely thick in 9/25 patients. In all patients with TCS, the EFs were coiled. Thus, quantitatively, the elastic fibers were decreased in 48 % of the patients, but the quality of the fibers was abnormal in 100 % of the patients with TCS.

Our initial interpretation of the histopathological findings of the first 25 patients with TCS and OTCS was that the FCT and elastic tissue of the fila were universally abnormal. Furthermore, the findings of abnormal elastic tissue potentially provided an explanation for why the macroscopically normal fila at surgery in patients with TCS might be less elastic and therefore more likely to tether the conus. However, in all our patients with TCS and OTCS, the coiling and thick elastic fibers were accompanied by cautery coagulation on H&E stains. This raised the possibility that the qualitative abnormalities seen, in particular fiber coiling, were related to cautery. On review of prior literature reports, it was noted that in all of the studies [10, 15, 19, 20, 26, 27] except one [5] where the procedure for isolating and transecting the filum was described,

Table 5 The findings on MRI and histopathology summarized

Filum findings	TCS (cautery used) <i>N</i> = 10	OTCS (cautery used) <i>N</i> = 15	TCS &OTCS(minimal cautery) <i>N</i> = 5
On MRI			
Thick (>2 mm) on MRI	10	4	1
Fat on MRI	5	1	3
On Pathology			
Fat	7	12	3
Glial tissue	4	1	2
Nerves	10	15	4
Ependyma	0	2	3
Ganglion cells	1	1	1
Dilated veins	4	7	1
Dense FCT	10	15	5
Focally decreased number of EF	4	7	1
Diffusely decreased number of EF	0	1	0
Coiled EF	10	15	0

FCT fibrous connective tissue, *EF* elastic fibers

the filum was cauterized prior to being cut. This prompted us to examine fila from five patients with TCS, in whom only minimal or no cautery was applied prior to obtaining the specimen of cut filum (group 4). In all of these patients, there was dense FCT in the fila, similar to what was found in the initial 25 patients. However, the coiling of EFs was no longer present. EFs were decreased in one patient, four had normal-appearing thin EFs, and one had thin EFs with a few thick fibers. These findings suggest that the abnormally thick and coiled EFs noted in the 25 patients with TCS in groups 1 and 2 were likely an artifact caused by the use of cautery. This would be akin to the EFs acting like stretched elastic bands (due to traction on the conus) which on cauterization and cutting would recoil, resulting in coiling and thickening. In one cadaver, the filum was cauterized in a similar fashion as at surgery (case 27 in controls) to see if the use of cautery might change the histopathological findings seen after death. In this patient, the histopathological findings were no different from other controls, where cautery had not been used. The FCT was loose with focal moderately dense areas and the EFs were evenly distributed, thin, and with no coiling. Thus, the coiling of the EFs after use of cautery may be a change seen in the living patient and may not be reproducible in the cadaver. These results call into question the validity of some of the changes noted in other studies of the filum when the specimen has been removed after use of cautery. It is probable that the changes described in the elastic fibers seen in the fila terminale from patients with TCS may be related to cautery coagulation and may not represent a genuine abnormality.

RFs (i.e., type 3 collagen fibers) were examined in the filum in 15 fetuses by Kural et al. [24] and were seen

ultrastructurally forming transversal fibers between the longitudinal type 1 collagen fibers described by Fontes et al. [22]. Kural et al. observed type 3 collagen fibers around the perineurium of peripheral nerves and the walls of the blood vessels. In our study, RFs were only seen in blood vessel walls and nerve twigs, similar to the findings by Kural et al. There was no convincing RFs in the fibrous tissue in any of the fila.

In addition to abnormal fibrosis in the fila in TCS, fat has been identified particularly in fila which are thick and where the conus medullaris is low lying [7, 26]. In our study, fat was identified histologically in 22/30 patients (groups 1, 2, and 3), and in 8 of these patients, the tissue resected was composed predominantly of fat. This is in contrast to fat only being identified in 9 of the 30 patients by MRI, 7/10 with low-lying and 2/20 with normal position conus. Thus, MRI is not as sensitive as histopathology in detecting fat in the filum. It is unclear in TCS whether with traction there is replacement of the normal constituents of the filum by fat thus reducing its elasticity, whether the adipose tissue forms adhesions which contribute to tethering of the filum, or is a marker of abnormal development of the filum [26].

Although the symptoms in TCS and OTCS may be similar, by imaging and histologically, there appears to be a spectrum of abnormality with a thicker filum and greater amount of fat in TCS and dense FCT in both TCS and OTCS. No trend in elastic fiber changes is certain in the absence of cautery.

Conclusions

Our results demonstrate that the fila in both TCS and OTCS are abnormal. These fila are constituted by dense FCTs and

increased fat deposition. While EFs were not clearly depleted versus control, they were abnormally thick and coiled where cautery was used prior to resection of the filum. The thick, coiled EFs were not seen when fila were removed with minimal cauterization, suggesting artifact. Since only five TCS specimens were subject to minimal cauterization, larger confirmatory studies would be useful.

Compliance with ethical standards Approval for the study was obtained from the Clinical Research Ethics Board of BC Children's Hospital and the University of British Columbia (H08-01919).

Conflict of interests The authors declare that they have no conflicts of interest.

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