A New Finding of a Tethered Cord in a Patient with Okamoto Syndrome

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Abstract:	We report a boy with Okamoto syndrome who presented to us at 11 year 3 months with bladder dysfunction and gait difficulties suggestive of Tethethered Cord Syndrome (TCS). To date, TCS has yet to be reported in the history of individuals with this syndrome. Okamoto syndrome is a congenital syndrome of unknown etiology characterized by severe mental retardation, growth failure, generalized hypotonia, congenital bilateral hydronephrosis, cardiac anomalies, cleft palate, and a characteristic facies. The patient subsequently underwent filum terminale sectioning with neuromonitoring for release of his cord. This surgery is relatively safe, and this patient saw a reversal of his TCS symptoms at follow-up clinical visits.
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Cover Letter

Okamoto syndrome is a congenital syndrome of unknown etiology, first recognized in two unrelated Japanese patients by Okamoto et al in 1997. The syndrome has thus far been marked by severe mental retardation, growth failure, generalized hypotonia, congenital bilateral hydronephrosis, cardiac anomalies, cleft palate, and a characteristic faciese. However, to date, there is no documentation in the literature of a tethered spinal cord in patients with Okamoto Syndrome. We present this new case of Tethered Cord Syndrome (TCS) in an 11 year old boy with already diagnosed Okamoto Syndrome to further broaden the picture of Okamoto Syndrome and enable thorough evaluation, identification of TCS, and early intervention in patients with this rare disease.

#The first author is a 4-year medical student. She is not a member of ASHG.

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Background

Okamoto syndrome is a congenital syndrome of unknown etiology, first recognized in two unrelated Japanese patients by Okamoto et al in 1997. The syndrome has thus far been marked by severe mental retardation, growth failure, generalized hypotonia, congenital bilateral hydronephrosis, cardiac anomalies, cleft palate, and a characteristic faciese. The rarity of Okamoto syndrome is highlighted by the fact that, to date, only three more cases have been noted. As such, little is known about the natural history and other features of Okamoto Syndrome beyond its main characteristics (Table 1).

For example, the fourth reported case presented with unilateral kidney hypoplasia and severe anal stenosis, new malformations that were not reported in the first cases (3). The fifth case had intestinal malrotation and uterine didelphysis, also new malformations not reported in earlier cases (7). Therefore, reports of new cases and follow-up of current ones will be helpful to understand the full spectrum of Okamoto and guide the management of patients with this syndrome.

Here, we report another new finding of a tethered cord in a patient with Okamoto syndrome. Tethered cord occurs when the spinal cord is fixed to tissues that restrict its movement within the spinal canal. Often, patients with this abnormality present with neurologic and urologic complaints such as back pain or bladder incontinence. Thus, identifying and correcting this problem can significantly improve the quality of life for these patients.

Case Presentation

We present an 11 year 3 months old boy who was the third case of Okamoto syndrome, first reported by Wallerstein et al (2005). He is of Chinese descent, born to parents with no known consanguinity. Genetic studies are unremarkable for any chromosomal abnormality. His prenatal history includes oligohydramnios with normal spontaneous vaginal delivery at 36 weeks gestation. At birth he was discovered to have severe bilateral hydronephrosis, hypotonia, ureteropelvic junction (UPJ) obstruction, cryptorchidism, cleft palate, ventricular septal defect (VSD), and bilateral hip dysplasia. Wallerstein et al, in his initial report on this patient at 2 months, noted non-specific changes in brain MRI but there was no mention whether an MRI of the spine was done. Later at 4 years old, an MRI of the spine revealed a syrinx at the T10-T12 level with a slightly enlarged conus but no note of a tethered cord (8). The images were not published to allow for a direct comparison with his follow-up imaging. The exam at that timed noted clonus but down-going plantar reflexes and diffuse hypotonia with severe motor delays and persistent incontinence. A renal ultrasound showed mild bilateral hydronephrosis and full bladder, with a post-void residual of 43cc and some decrease in the hydronephrosis after voiding. No urodynamics were reported from this time period.

At 8 years and 7 months old the patient's neurologist noticed a sacral dimple and ordered repeat spine imaging. He still had the characteristic facies of Okamoto syndrome with severe hypotonia, but with a syrinx now extending from approximately T10 to the tip of the conus medullaris at L2 and a newly diagnosed tethered spinal cord (Figures 1 and 2).
Surgery was recommended for the patient at that time, however there was no follow-up. At 11 years 3 months the patient presented with back/leg pain with severe gait difficulty, lower

extremity paresthesia, numbness, and weakness with worsening bladder dysfunction.

This new bladder dysfunction was in addition to his long history of urological problems. The patient at 4 months had left ureteropelvic junction obstruction and bilateral hydronephrosis with grade IV to V bilateral reflux. Since then, he had a pyeloplasty, bilateral ureteral reimplantation and follow-up studies have shown a persistent, stable, mild hydronephrosis. He presented to us with a neurogenic bladder, secondary to his tethered cord. Voiding cystourethrogram (VCUG) confirmed a large capacity bladder with premature opening of the bladder neck.

The patient subsequently underwent a filum terminale sectioning with neuromonitoring to release the cord. A partial laminectomy at L3/4 below the conus gave adequate exposure of the intradural contents to dissect the filum terminale from the cauda equina. Neurostimulation positively identified the nerve roots with detectable responses in the distal musculature, including the sphincter. The filum terminale itself showed no response with stimulation, and was easily identified but its different color and accompanying blood vessels. A portion was resected to release the tether on the conus, and to decrease the risk of recurrent tethering. The dura was subsequently closed and a valsalva maneuver is done to ensure no CSF leak (Figures 5 and 6).

The patients showed marked neurologic improvement post-operatively. At his 6-month follow-up, he reported less leg pain with increased strength in his lower extremities and much improved gait. However, improvement in his bladder function was not noted until at his 10-month follow-up visit. His urinary symptoms continue to improve now 2 ½ years after surgery, and he ambulates independently.

Discussion

Tethering of the spinal cord results from abnormalities of the filum terminale which restrict the mobility of the conus medullaris. Normally, the filum terminale is an elastic extension of the pia matter proceeding downward from the conus medullaris; its elasticity allows the free movement of the spinal cord during extension and flexion of the spine. However, compromise of the filum terminale and subsequent tethering of the spinal cord prevents the conus medullaris from ascending to its normal adult position at L1-L2, resulting in stretching and damaging of nerve fibers and blood vessels over time (5). Tethered Cord Syndrome (TCS) is the constellation of symptoms and abnormalities that can result from such compromise. Patients may have a minimal tethered cord that does not cause symptoms until further growth or trauma cause increased stretch on the conus (2).

The presentation of TCS varies with age (2). Toddlers and children tend to present with both motor and sensory dysfunction, and regression in developmental milestones is often the presenting symptom of a tethered cord. Certain cutaneous stigmata such as midline hypertrichosis, dermal sinus tracts, or in this patient's case, a sacral dimple are usually the signs that alert physicians to look for an underlying tethered cord. In late childhood and in adults with a known history of spina bifida, non-dermatomal pain, sphincter dysfunction and incontinence, exacerbated by flexion and extension of the spine are usually the presenting complaints.

In all age groups, however, bladder dysfunction is a predominant symptom. In fact, bladder dysfunction plays an important role in the initial diagnosis of a tethered cord and is used as a measurement of worsening or improvement following detethering surgery. This is the case for this patient as, in addition to his stable congenital hydronephrosis, he also presented with bladder incontinence, secondary to a neurogenic bladder. The evidence of a full bladder and a relatively large PVR at age 4 may have been an early sign of the tethering.

The most common cause of a neurogenic bladder in the pediatric population is a spinal dysraphism (1). These spinal anomalies lead to bladder sphincter dyssynergy (1) - the main problem in a neurogenic bladder- and releasing the tether often restores sphincter function. The improvement in bladder function after detethering has been as great as 50% (2).

Besides improvement in bladder function, other studies report up to 91% decrease in fecal symptoms (6). Back, leg pain, and paresthesias also see improvement with resultant significant improvement in gait function as well. For some patients, however, scarring with recurrent TCS does occur, and the prevalence is highest for patients between 6 to 13 years old (6). Thus, patients who have undergone cord release require regular follow-up to check for retethering.

Therefore, neurosurgical intervention is recommended in most patients (especially pediatric patients) presenting with TCS to prevent further urologic and neurologic deterioration, although the ideal time to correct the problem is still debatable.

Conclusion

The incidence of a tethered cord in patients with Okamoto syndrome remains unknown for now. However, with this knowledge of a possible tethered cord in these patients, future patients identified with Okamoto syndrome should receive a complete evaluation of their brain and spine, with careful attention to any cutaneous stigmata suggesting the need for further evaluation with imaging of the spine and urologic evaluation for possible tethered cord. Furthermore, as this patient demonstrates, these evaluations should continue, at least until growth is complete, as patients with an underlying tethered cord can develop worsening symptoms later in childhood that were previously mild.

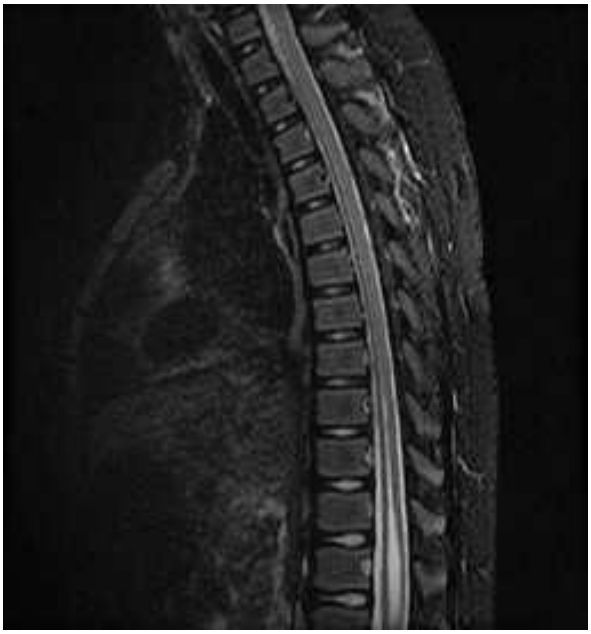

Figure 1: pre-operative view of syrinx

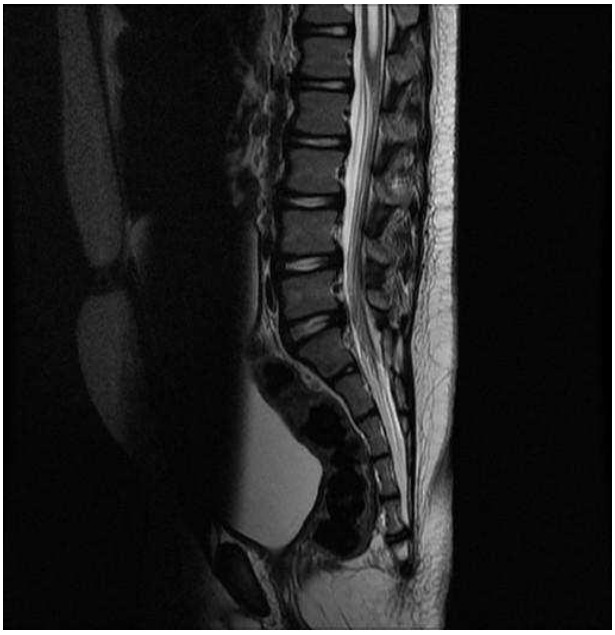

Figure 2: pre-operative view of filum terminale

Figure 3: post-operative view of syrinx

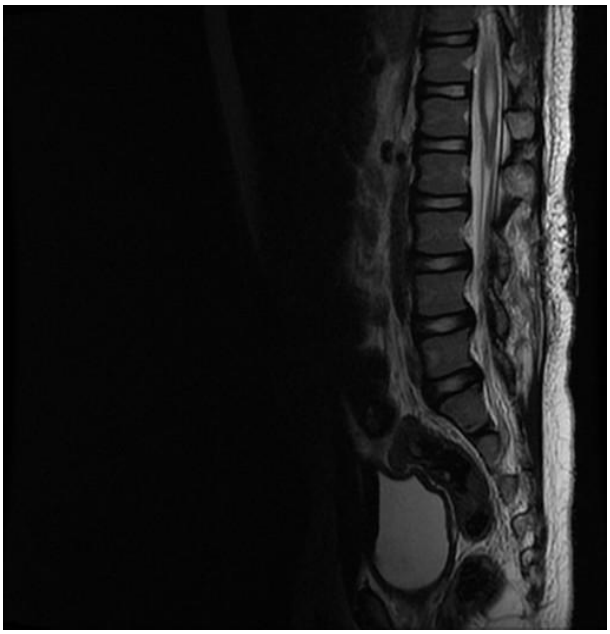

Figure 4: post-operative view of filum terminale

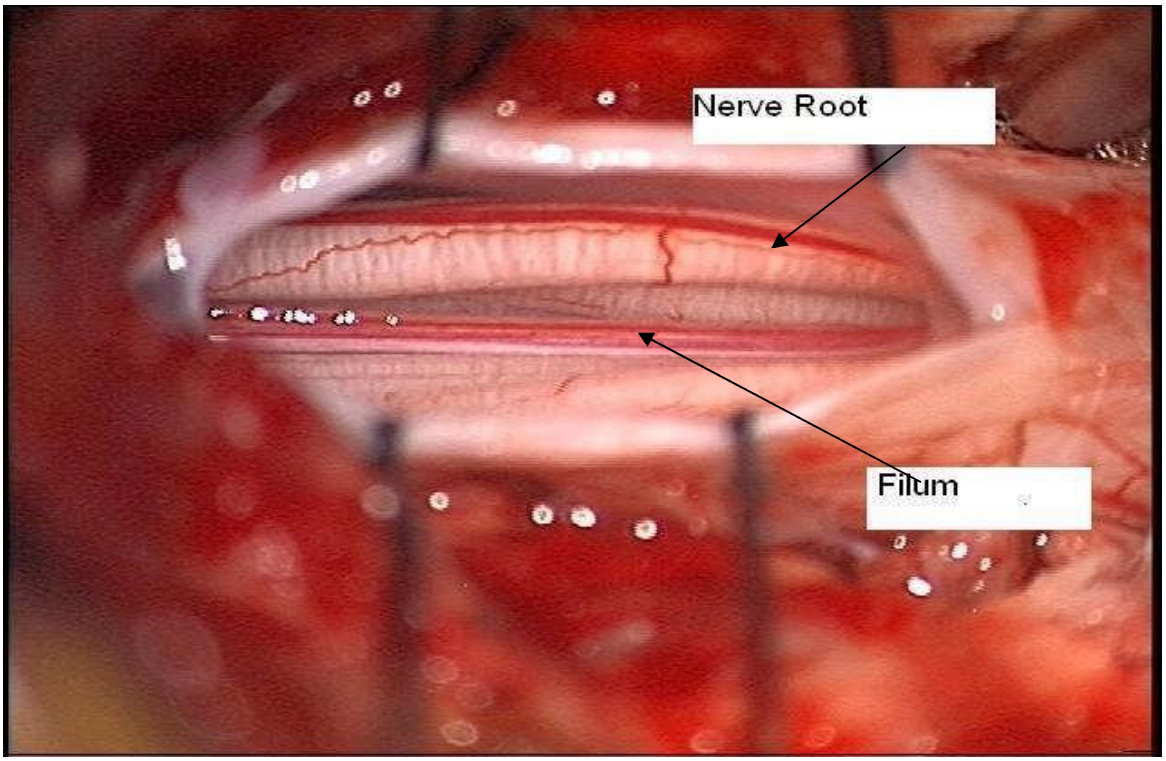

Figure 5: pre-release view of filum terminale

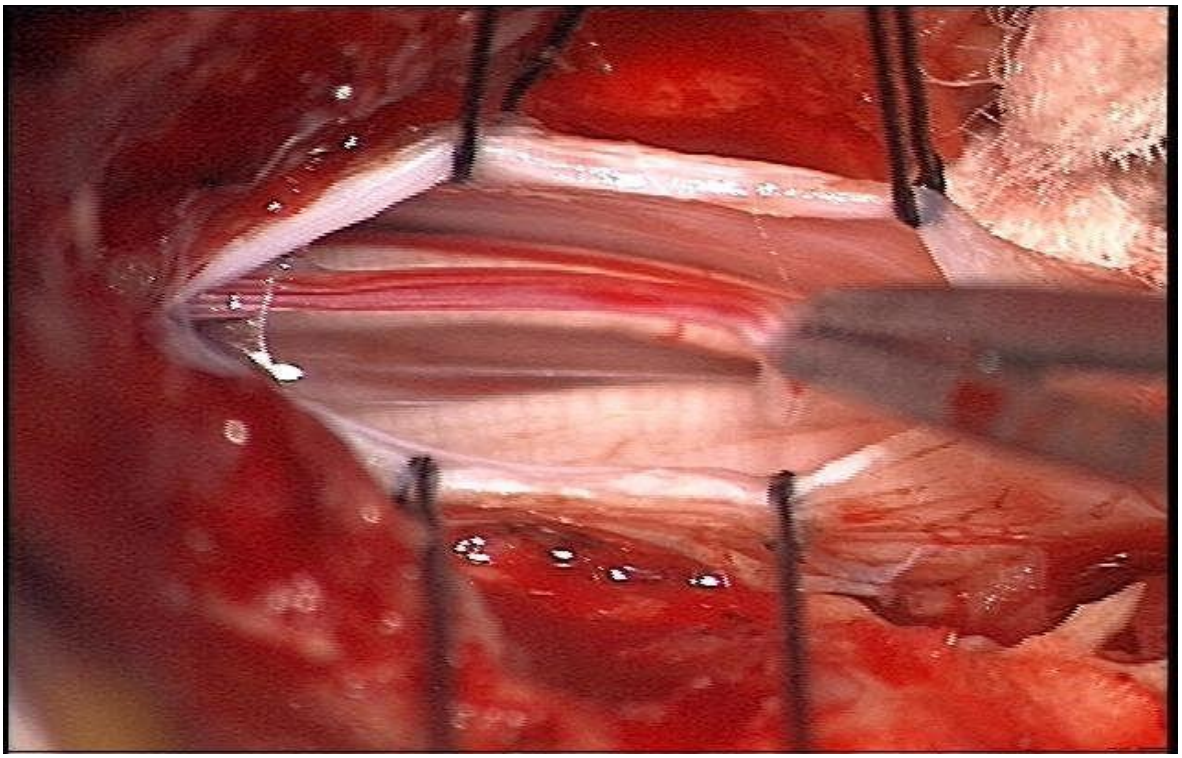

Figure 6: post distal release of filum terminale, prior to proximal severing of filum from the conus medularis

Summary of Previous Findings in Okamoto Syndrome

	Okamoto et al, 1997	Okamoto et al, 1997	Wallerstein et al, 2005	This report	Markouri et al, 2008	Taylor & Aftimos
Age at exam	2 y	15m	3m	8y7m	5-36m	Birth to 12d
Hypotonia	+	+	+	+	+	+
Intellectual disability	+	+	+	+	+	n/a
Growth failure	+	+	+	+	+	n/a
Microcephaly	+	+	+	+	+	_
Midface hypoplasia	+	+	+	+	+	+
Downturned mouth	+	+	+	+	+	+
Upturned nose	+	+	+	+	+	+
Flat nasal Bridge	+	+	+	+	+	+
Short nose	+	+	+	+	+	+
Hypertrichosis	+	+	_	_	+	+
Long ear lobe	+	+	+	+	+	+
Cleft palate	+	+	+	+	+	+
Open mouth	+	+	+	+	+	+
Webbed neck	+	+	_	_		+
Hydronephrosis	+	+	+	+	+	+
UPJ obstruction	+	+	+	+	+	+
Cardiac anomaly	+	+	+	+	+	+
Hypermobile joints	+	+	+	+	+	+

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