Natural History of Occult Spinal Dysraphism

3

Jeffrey P. Blount and Zachary G. Wright

Abbreviations

DST	Dermal sinus tract
OSD	Occult spinal dysraphism
SCM	Split cord malformation
TCS	Tethered cord syndrome

Introduction

The natural history of OSD is the central issue impacting surgical decision-making in occult dysraphism. Only by comparing surgical risks to the natural history of the untreated illness can a rational, informed decision be made for or against surgical intervention. While the detailed natural history of the three broad forms of OSD (lipoma, DST, SCM) remains incompletely understood, the overall clinical pattern appears dominated by the tethered cord syndrome (TCS). There is some controversy surrounding whether TCS is the sole or a dominant contributor to clinical decline in patients harboring an OSD, but there is consensus that it is a potentially treatable important contributor in many OSD patients.

J. P. Blount (✉) · Z. G. Wright
Pediatric Neurosurgery, Children's of Alabama, Birmingham, AL, USA
e-mail: jeffrey.blount@childrensal.org

R. S. Tubbs et al. (eds.), *Occult Spinal Dysraphism*,
https://doi.org/10.1007/978-3-030-10994-3_3

Background

During the 1950s, papers described neurological decline over time associated with occult dysraphism, but it was not until the 1970s that surgical procedures were developed and widely performed that attempted to disrupt the tether and arrest such decline [1–4]. Patients harboring OSD defects were found to show neurological disability that generally correlated with age for the first two decades of life [5, 6]. This recurring observation in multiple series prompted the concept of reversible decline arising from progressively severe tethering of the spinal cord [5–9].

Patients who presented with neurological findings demonstrated arrest of decline and even modest improvement following surgical untethering in multiple large clinical series [5, 6, 10–14]. An improvement in pain and cessation of neurological decline were observed in many symptomatic patients regardless of the type of occult defect present. Despite confounders and methodological limitations to these studies, a period of robust enthusiasm ensued for the concept of TCS and the effectiveness of surgery in disrupting it [10, 15–17]. Patients with symptoms showed good response to surgery but more overall neurological disability than those who were operated upon before symptoms developed [7]. This was widely interpreted as demonstrating the importance of early surgery, and enthusiasm for prophylactic surgery and early referral increased [6, 7]. It became generally accepted that asymptomatic occult lesions were associated with inevitable decline and that surgical untethering was the best way to prevent this and the associated loss of function and independence [6, 7, 16, 18, 19].

Over time, the long-term effectiveness of surgery in preventing decline from TSC became less clear [20, 21]. A disconcerting number of patients with lipomas demonstrated signs and symptoms of recurrent TSC following prophylactic untethering [21, 22]. This called into question the long-term effectiveness of surgical untethering in protecting against neurological decline related to tethering. Some groups found that lipoma patients who were serially examined without surgical intervention demonstrated stable neurological exams or nearly imperceptible rates of decline [23]. This prompted a reassessment of the inferred natural history that had been accepted, and several groups adopted and advocated a more conservative approach toward asymptomatic patients with lipomas [20, 24, 25]. Understanding of the natural history of OSDs remains controversial and is of great practical surgical relevance since it shapes the fundamental approach to prophylactic surgery and its role. Since most children are screened by pediatricians and are referred for any cutaneous anomaly involving the lumbar region, this is the most common clinical scenario and as such has great practical importance.

Overview of the Natural History of OSD

While there is general consensus among experienced observers that tethering is important in the decline of patients with OSD, there is disagreement about its relative contribution and its variability in asymptomatic patients [20, 22]. Furthermore, there are pronounced disparities in opinion among highly experienced, thoughtful

investigators with regard to the aggressiveness of resection of tethering lesions [14, 16, 23]. Much is uncertain and there can be confusion. A clear summary of central principles and areas of uncertainty and future investigation is worthwhile:

Established Principles of the OSD Natural History

1. Progressive neurological decline of the lower extremities and bladder/bowel during the first two decades of life is a real and predictable phenomenon for most patients who harbor a form of OSD [5–7, 13, 22].
2. Patients may show different rates and extents of decline and up to slightly less than half with asymptomatic lipomas may decline only modestly over time or demonstrate clinical stability [20, 23, 24, 26]. Split cord malformations may similarly show some variability in decline that is currently less well established [12, 15, 18, 27].
3. The loss of neurological function is typically not recovered [5, 9, 12, 22, 28].
4. Decline is often subtle and occurs over multiple domains (motor, sensory, pain, bladder reflexes, etc.) that vary between patients [10, 17, 20, 22, 28]. A useful classification of clinical patterns of decline has never been developed.
5. Objective measures of lower extremity function or the status of neuro-urological health are lacking. Current measures are imperfect and subject to interpretation and subjectivity [14, 22, 24].
6. Surgical intervention for patients with symptoms seems to help [5, 18, 22, 27–29]:
   - Pain is improved most reliably.
   - Neurological decline is arrested at least transiently, but lost function rarely improves or returns.
   - Recurrent late decline occurs in a significant percentage of patients with lipomas who undergo surgery via traditional surgical approaches (sub-total placode reconstruction).
   - Despite limitations in metrics, patients who are carefully followed with multidisciplinary assessments do better than those who are lost to follow-up.

Central Questions Regarding the Natural History of OSD

1. To what extent are variations in clinical natural history due to the following?
   - Pathological anatomy
   - Phenotypic expressions of subtle genetic differences (molecular subtype analysis and classification) between different types of tethering mechanisms
   - Epigenetic phenomena such as activity, obesity, BMI, diet, metabolism, diet or toxin exposure
2. Is the fundamental event in the pathogenesis of tethered cord related to:
   (a) Longitudinal stress imparted by growth?
   (b) Fixation with micro-trauma from repeated movements of normal living?
   (c) Absorption of the pulsatile force of a large blood volume with systole?

3. How variable is the rate of decline and do different tethering lesions result in similar rates of neurological decline?
4. Are the lesions that show clinical progression different in some definable way from those that show clinical stability?
5. Is the mechanism of decline in recurrent cases of tethered cord the same as that for initial de novo tethered cord?
6. Are radical resection techniques of lipoma resection (advocated by Pang and colleagues) widely applicable/achievable in a diverse and broad community of pediatric neurosurgery?

Natural History of Dermal Sinus Tracts

Congenital dermal sinus tracts are thought to arise from focal failure of disjunction between the neuroectoderm and cutaneous ectoderm during the first trimester [1, 22, 30, 31]. The result is a focal tract between the skin and underlying neural structures. The clinical spectrum is wide, but this lesion threatens neurological well-being as (a) a source of tethering and (b) a potential conduit between the subarachnoid space and the external world. Thus, it can cause decline from TSC or can potentiate bacterial meningitis [1]. DSTs have been reported on the midline along the entire length of the neuraxis from the nose to the sacrum, but the overwhelmingly most common location for this rare lesion is over the lumbar or lumbosacral regions [1, 30]. Critical characteristics that distinguish DSTs from sacral pits include skin origination within the gluteal crease, termination within the central nervous system, lining with stratified squamous epithelium, and other concomitant cutaneous anomalies [1, 30]. Because these lesions entail a real and well-understood risk of infection, they are virtually always removed [22]. Therefore, the natural history of untreated dermal sinus tracts has never been comprehensively studied or reported in the modern era. However, historical studies show that untreated DST could give rise to a wide range of infections including meningitis and focal abscesses [1, 31]. Virtually all of these reports are case reports or limited small series, so the natural history and exact incidences of comorbidities complicating DST have never been calculated. However, from a practical perspective, natural history is a less important issue because DSTs present a real risk of recurrent meningitis [22]. Their surgical removal is low risk, and virtually all that are diagnosed are surgically removed in North America [1, 22, 30].

Natural History of Split Cord Malformations

SCMs are rare forms of closed dysraphism characterized by division of the spinal cord into either a single cord divided by a septum (type I, previously diastematomyelia) or formation of two hemi-cords variably interrupted by a fibrous or bony septum (type II, previously diplomyelia) [3, 11, 15, 27, 29]. The embryo-pathogenesis is uncertain, and various hypotheses have been proposed. Previously, the terms

diplomyelia and diastematomyelia were used inconsistently and occasionally interchangeably, precluding historical contributions to specific natural history studies [12, 18, 32]. Collectively and from a practical surgical perspective, the various forms of SCM are strongly associated with TCS and therefore potentially surgically amenable to improving an otherwise threatening natural history. In a true split cord (SCM I), tethering can occur via either a perforating bony or cartilaginous spicule, the associated thickened arachnoid bands, or by the medial dural sleeve that can envelop the perforating spur [15, 18, 29]. There are too few series for the natural history of these lesions to have been established. However, recurring observations are similar to other tethering lesions. Guthkelch was an early proponent of observation in an effort to avoid harm [3]. Early patients were observed and deteriorated neurologically, while later patients were operated upon "prophylactically" and retained normal function [3]. These observations established a consensus for the central role of tethering in the pathophysiology of SCMs and the inferred ominous natural history of the untreated condition.

More recent studies have suggested other possible contributors to the pathophysiology. Andar and colleagues concluded from studying a cohort of 47 patients with split cord anomalies that the "neuro-orthopedic syndrome" characterized by sensory-motor dysfunction and lower limb asymmetry was a consequence of abnormal functional anatomy and was minimally amenable to surgical improvement [27]. Neurological and "neuro-ortho" findings were common, but true progression of symptoms was rare. Surgical untethering for true progression was effective in arresting but not reversing the observed declines [27]. Thematically, this is similar to other examples of TSC from OSD. Early observations of decline in patients harboring potentially tethering lesions supported a fundamentally essential role for surgery in arresting ongoing decline. Greater experience modestly tempered these inferences by enhancing awareness that each of these dysraphisms is a complex lesion with inherently disordered embryogenesis and resulting disordered neuroanatomy. Tethering appears to be an important potential contributor but is unlikely to be the only one. Consequently, surgical untethering is contributory but can neither reverse deficit nor prevent all neurological impairment.

Natural History of Spinal Cord Lipomas

Lipomas are the most common form of OSD and consist of fat and fibrous masses that invade and tether the spinal cord [6, 25, 33]. They are comprehensively discussed in Chap. 11 and will be considered briefly here with particular regard for their natural history. Lipomas of the filum (Chap. 8) (filar lipomas) minimally invade the neural structures but can cause tethering of the spinal cord irrespective of whether the position of the conus medullaris is abnormally caudal [2, 10, 21, 33]. The natural history of these lesions has never been studied in detail, but they are observed in 5% of otherwise normal lumbar MRIs [33]. It therefore seems that a substantial percentage of these lesions never cause symptoms and require no intervention [21, 33]. It has been inferred that robust thickened fila with fatty infiltration

show characteristic decline associated with TCS, particularly if the conus is abnormally caudal in position [2, 4, 17]. In virtually all surgical series, surgical clipping of the fat-infiltrated filum in patients with symptomatic TCS is associated with reduction or dissipation of pain, cessation of neurological decline, and minimal operative morbidity. The entity of TCS with conus in the normal position has been described and debated and is developed elsewhere in this book (Chap. 8). The natural history of this entity is unknown.

Lipomas of the conus are markedly more complex. They are anatomically very variable and can be challenging both for clinical decision-making and technical performance of the resection/untethering. Dorsal lipomas invade directly into the dorsal surface of the conus and spare the exiting nerve roots. In contrast, caudal and transitional lipomas incorporate the distal caudal surface of the conus, which involves the exiting nerve roots in the fat mass [6, 14, 16, 17]. These challenges and the resultant potential for iatrogenic neurological injury have prompted many neurosurgeons to adapt a limited approach to fat removal. In a conventional resection for a conus lipoma, fat is removed to enable debulking and enlargement of the surrounding dural sleeve, but aggressive resection at the interface between fat and spinal cord is not pursued [6]. An alternative approach prompted by dissatisfaction with the rates of recurrent tethering incorporates a more radical resection of fat and reconstruction and expansion of the dural sleeve to prevent re-tethering [8, 25]. Radical resection and reconstruction of the dural sleeve shows better progression-free survival from neurological decline but has been embraced in a limited way owing to its inherent technical challenges and risks of dissecting at the interface between the lipoma and the conus medullaris.

The natural history of lipomas is widely considered to represent TCS. Older patients with lipomas in their first two decades have been found in multiple series to harbor more neurological disability than infants and young children. Only a few series distinguish symptomatic from asymptomatic patients and incorporate both operative and observation treatment arms. Tu et al. demonstrated that in a cohort of patients without deficit, those who were observed without surgery showed a 79% rate of progressive neurological decline, whereas those who underwent prophylactic untethering demonstrated a 30% rate of decline at 5 years [14]. Among patients with a fixed deficit, 80% went on to develop a deficit, whereas only 40% of those who had untethering surgery demonstrated decline [14]. Valentini and colleagues reported an operatively treated cohort, 44% of which demonstrated preoperative progressive decline [19].

Despite these widely accepted concepts, it remains likely that multiple factors are involved and that tethering is not the only explanation for the observations. This has been embraced by investigators who advocate the more conservative approach of waiting for convincing clinical signs of decline before intervening operatively [14, 20, 23, 24]. Key observations that support this interpretation and approach include:

1. The development of signs and symptoms is likely to be a matter of emergence and recognition as well as development or progression; examination of the lower extremities and bladder in infants and young children is notably difficult.

2. As more groups have carefully examined young children, it is apparent that the incidence of baseline neurological dysfunction is higher than previously supposed. Neurological dysfunction seems to arise as a result of fundamentally disordered anatomical development in addition to whatever elements of tethering are present.
3. There is clear variation in progression between patients so that it is likely that no single pathophysiological pathway is implicated.
4. Older asymptomatic children who were never treated are also not considered in the analyses of natural history arising from outcome studies of early treated patients. This important omission impedes accurate assessment of the effectiveness of prophylactic surgery.
5. Age could contribute in pathophysiological processes other than tethering as it does in many other body systems.

The more conservative, expectant approach for asymptomatic lipomas resulted in observed decline and need for intervention in only 21% at a mean 5.9 years follow-up of the cohort managed and observed at the Great Ormond Street Hospital for Children in London [23]. By 10 years of follow-up, the cumulative risk of decline was only 40%, which could imply that more than half of prophylactic procedures for asymptomatic lipomas are unnecessary [23]. This is particularly noteworthy because longitudinal studies of cohorts of asymptomatic patients operated on for lipomas have demonstrated late deterioration of function and the development of symptoms over time in significant numbers [9, 21, 23, 34]. This has cast doubt on the effectiveness of prophylactic surgery in conferring long-term protection against neurological decline. When the large series from Paris was reviewed, an actuarial risk of 60% for delayed decline was observed in patients who underwent prophylactic surgical untethering by conventional methods [21]. This contrasts sharply with outcome data published by Pang in a series of consecutive manuscripts that chronologically detailed his cumulative experience with techniques of radical lipoma resection and dural sleeve reconstruction. The progression-free survival observed in 315 patients with these techniques was 88% at 20 years overall and 99% for previously untouched lipomas [8, 25]. However, these techniques have been embraced by few others because of their perceived inherent operative risks and technical demands.

The Way Forward

Surgical Decision-Making

The individual surgeon or clinician must establish his/her preferred approach on the basis of training, experience, technological support, technical capability, and understanding and interpretation of the natural history of these conditions. There is nearly uniform consensus that tethering contributes to decline in patients harboring OSD lesions such that operative untethering is recommended for symptomatic patients. Contemporary surgical and technological adjuncts including the operating microscope

and intraoperative nerve monitoring contribute significantly and are important for reducing risk of iatrogenic injury. Complete untethering and the patulous space between the cord and dura are surgical principles important for interrupting the natural history of the OSD lesions. While untethering operations are generally very safe, careful informed consent should allude to risks of neurological injury, wound-related problems (including possible need for re-operative closure), CSF leaks, infection, bleeding, and loss of effectiveness of the operative procedure over time.

The approach to the asymptomatic patient is more complex. Dermal sinus tracts threaten the patient by both tethering and potential infection so they are uniformly operated upon at diagnosis. Similarly, the role of tethering is widely agreed to impart serious, preventable threat in split cord malformations (SCMs). Further, the site of tethering is focal in SCMs so that most centers appear to support operative untethering before symptoms in the SCMs. For lipomas, more nuance is required in decision-making. Lipoma patients appear to deteriorate with time, but there are variations in the rate and extent of decline, and there is variability in natural history. Furthermore, the role for conventional (limited resection) surgery to prevent decline appears transient in at least some patients. This is inferred from symptomatic patients who have undergone untethering and exhibit recurrence of symptoms after a period of arrest of deterioration.

Conventional surgical untethering arrests decline at least transiently for most patients. The role for more radical resection for asymptomatic patients is more controversial. Pang's large series show that radical resection with reconstruction of the dural sleeve offers the best-reported long-term outcomes with near cure for dorsal and transitional lipomas. The greatest challenge of this work is that sub-total resections of lipomas fared no better or marginally worse than unoperated lipomas over time. The contrast in outcomes between sub-total and radical resections of lipomas is stark.

Despite Pang's claim that the techniques can be learned and perfected by any neurosurgeon, the current literature provides scant evidence that this has occurred so far [8]. Only limited, retrospective, single-institution series from outside of North America have documented outcomes with radical resection [19]. Nonetheless, this work appears to have significantly affected the way in which lipomas are approached in that many surgeons seem increasingly aggressive in reducing the mass of fat present in such lesions and in reconstructing a patulous dural sleeve. The extent to which radical techniques are embraced is a highly personal decision for each surgeon and team that must reflect their training, experience, technological support, and interpretation of the best available techniques.

Future Directions: Investigation and Study Design

The value of retrospective single-institution centers in elucidating the natural history of occult defects is modest. Study design with greater power and scope will be needed to answer these central questions. A multicenter prospective registry, such as the National Spina Bifida Patient Registry (NSBPR) which is supported by the US

Center for Disease Control (CDC), could be an appropriate starting point. Characterization and classification of large numbers of lipomas and their response to treatment could reveal differences that are currently not appreciated. Longitudinal observations of prospectively compiled cohorts over long follow-up times will be required to provide data that will enhance our understanding of the natural history of the tethering lesions. The genetic profile of each lesion must be determined, studied, and recorded. The development of alternate classification schemes that reflect molecular differences between lipomas should be evaluated and encouraged if promising.

Standardized, validated, objective metrics of outcome are also needed. At present, all available outcome parameters for evaluating tethered cord and neurological function are subjective. There is no disease-specific validated outcome measurement for dysraphism. The ultimate objective would be standardized, validated measures that are not performed by the treating team. Only when large cohorts of patients with OSD lesions are followed longitudinally with the best available metrics will the true natural history of the OSD conditions be known with certainty.

References

1. Ackerman LL, Menezes AH. Spinal congenital dermal sinuses: a 30 year experience. Pediatrics. 2003;112:641–7.
2. Goldberg C, Fenelon G, Blake NS, Dowling F, Regan BF. Diastematomyelia: a critical review of the natural history and treatment. Spine. 1984;9:367–72.
3. Humphreys RP, Hendrick EB, Hoffman HJ. Diastematomyelia. Clin Neurosurg. 1983;30:436–56.
4. LaMarca F, Grant J, Tomita T, McLone DG. Spinal lipomas in children: outcome of 270 procedures. Pediatr Neurosurg. 1997;26(1):8–16.
5. Guthkelch AN. Diastematomyelia with median septum. Brain. 1974;97:729–42.
6. Pang D, Zovickian J, Oviedo A. Long-term outcome of total and near-total resection of spinal cord lipomas and radical reconstruction of the neural placode- part I- surgical technique. Neurosurgery. 2009;65(3):511–28.
7. Patil PS, Gupta A, Kothari PL, Kekre G, Gupta R, Dikshit V, et al. Immediate and long-term outcome analysis of lipomyelomeningocele repair in asymptomatic infants in a tertiary care center. J Pediatr Neurosci. 2016;11(2):99–104.
8. Proctor MR, Scott RM. Long term outcome for patients with split cord malformation. Neurosurg Focus. 2001;10(1):1–5.
9. Radmarresh F, Nejat F, El Khashab M. Dermal sinus tract of the spine. Childs Nerv Syst. 2010;26:349–57.
10. English WJ, Maltby GL. Diastematomyelia in adults. J Neurosurg. 1967;27:260–4.
11. Garceau GJ. The filum terminale syndrome (the cord-traction syndrome). J Bone Joint Surg Am. 1953;35-A(3):711–6.
12. Kanev P, Bierbrauer K. Reflections on the natural history of lipomyelomeningocele. Pediatr Neurosurg. 1995;22:137–40.
13. Tuite GF, Thompson DNP, Austin PF, Bauer SB. Evaluation and management of tethered cord syndrome in occult spinal dysraphism: recommendations from the children's continence society. Neurourol Urodyn. 2018;37(3):890–903.
14. Veenboer PW, Bosch JL, van Asbeck FW, de Kort LM. Paucity of evidence for urinary tract outcomes in spinal dysraphism: a systemic review. BJU Int. 2013;112(7):1009–17.

15. Jindal A, Mahapatra AK. Split cord malformations- a clinical study of 48 cases. Indian Pediatr. 2000;37:603–7.
16. Morris KM, Findlay GF. Dysraphic problems in the lumbar spine: dilemmas in management – a review of 49 cases. Eur Spine J. 1992;1(2):105–8.
17. Tu A, Hengel AR, Cochrane DD. The natural history and management of patients with congenital defects associated with lumbosacral lipomas. Childs Nerv Syst. 2016;32(4):667–73.
18. Tseng JH, Kuo MF, Kwang TY, Tseng MY. Outcome of untethering for symptomatic spina bifida occulta with lumbosacral spinal cord tethering in 31 patients: analysis of pre-operative prognostic factors. Spine J. 2008;8(4):630–8.
19. Wykes V, Desai D, Thompson DN. Asymptomatic lumbosacral lipomas- a natural history study. Childs Nerv Syst. 2012;28(10):1731–9.
20. Cools MJ, Al-Holou WN, Stetler WJ, Wilson TJ, Maraszko, et al. Filum terminale lipomas: imaging prevalence, natural history and conus position. J Neurosurg Pediatr. 2014;13:559–67.
21. Rapal S, Salamat MS, Tubbs RS, Kelly DR, Oakes WJ, Iskander BJ. Tethering tracts in spina bifida occulta: revisiting an established nomenclature. J Neurosurg Spine. 2007;7:315–22.
22. Jones PH, Love JG. Tight filum terminale. AMA Arch Surg. 1956;73:556–66.
23. Cochrane DD. The patterns of late deterioration in patients with transitional lipomyelomeningocele. Eur J Pediatr Surg. 2000;10(Suppl 1):13–7.
24. O'Neill P, Singh J. Occult spinal dysraphism in children: need for early neurosurgical referral. Childs Nerv Syst. 1991;7(6):309–11.
25. Pierre-Kahn A, Zerah M, Renier D, Cinalli G, Sainte-Rose C, Lellouch-Tubiana A, et al. Congenital lumbosacral lipomas. Childs Nerv Syst. 1997;13:298–335.
26. Valentini LG, Selvaggio G, Erbetta A, Cordella A, Pecoraro MG, et al. Occult spinal dysraphism: lessons learned by retrospective analysis of 149 surgical cases about natural history, surgical indications, urodynamic testing and intraoperative neurophysiologic monitoring. Childs Nerv Syst. 2013;29(9):1657–9.
27. Andar UB, Harkness WF, Hayward RD. Split cord malformations of the lumbar region. A model for the neurosurgical management of all types of 'occult' spinal dysraphism. Pediatr Neurosurg. 1997;26(1):17–24.
28. Wright RO. Congenital dermal sinuses. Progr Neurol Surg. 1971;4:175–91.
29. Iqbal N, Qadeer M, Sharif SY. Variation in outcome in tethered cord syndrome. Asian Spine J. 2016;10(4):711–8.
30. Tu A, Hengel AR, Cochrane DD. Radiographic predictors of deterioration in patients with lumbosacral lipomas. J Neurosurg. 2016;18(2):171–6.
31. Averbeck MA, Madersbacher H. Follow up of the neuro-urological patient: a systematic review. BJU Int. 2015;115(Suppl 6):39–46.
32. Ersahain Y, Mutluer S, Kocaman S. Split cord malformations in children. J Neurosurg. 1998;88:57–65.
33. Cornette L, Verpoorten C, Lagae L, Van Calenbergh F, Plets C, Vereecken R, Casaer P. Tethered cord syndrome in occult spinal dysraphism: timing and outcome of surgical release. Neurology. 1998;50(6):1761–5.
34. Pang D, Zovickian J, Wong ST, Hou YJ, Moes GS. Surgical treatment of complex spinal cord lipomas. Childs Nerv Syst. 2013;29(9):1485–513.