

# The Absence of the Neuronal Component in Limited Dorsal Myeloschisis: A Case Report

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## Established Facts

- The presence of neuroglial tissue is considered a hallmark of limited dorsal myeloschisis (LDM).
- Several authors report cases of LDM in which neuroglial tissue cannot be demonstrated, and they collectively indicate that neuroglial tissue is probably present in the unresected part of the stalk.

## Novel Insights

- We describe a case of limited dorsal myeloschisis (LDM) in which, despite extensive resection, neuroglial tissue is not observed histopathologically. Here, we propose that in some cases of LDM, no neuroglial tissue might be present whatsoever.
- We provide an alternative hypothesis for the embryo-pathological origins of LDM that explains the absence of neuroglial tissue in some cases of LDM.

## Keywords

Spinal dysraphism · Limited dorsal myeloschisis · Glial fibrillary acidic protein

## Abstract

**Introduction:** The presence of neuroglial tissue is considered a hallmark in limited dorsal myeloschisis (LDM). However, several reports have indicated that the presence of neuroglial tissue in LDM cannot always be demonstrated. Here, we present such a case of LDM and provide an alterna-

tive hypothesis for lacking the neuronal component. **Case Description:** An antenatal LDM suspected neonate was born with a cystic skin lesion and membranous sac typical for membranous LDM. Three days postpartum the otherwise healthy infant underwent surgery, during which the stalk was resected and the spinal cord was untethered. Histopathologically, no neuroglial tissue could be determined. Noteworthy, S-100 staining revealed numerous peripheral nerves. **Discussion:** The current paradigm explains the absence of neuroglial tissue in resected stalks of LDM by indicating that it should be present in the unresected part, more proximal

to the dorsal spinal cord. We hypothesize a different mechanism in which following reopening of the neural tube, mesodermal invasion causes a tight and persistent strand between the cutaneous- and neuroectoderm. Elongation of this mesodermal strand during embryological development allows for the formation of a mesenchymal stalk without the presence of neuroglial tissue. Hydrodynamic forces can cause fistulation of the poorly differentiated mesodermal tissue and subsequently lead to a sacular defect.

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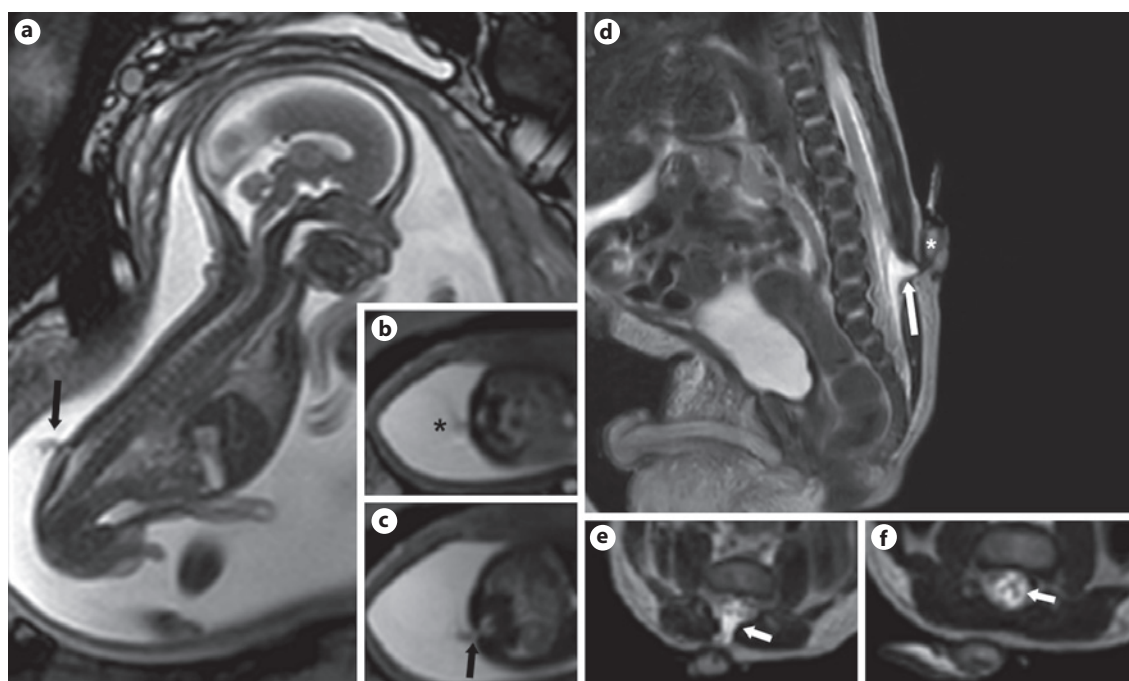
## Introduction

Limited dorsal myeloschisis (LDM) is a form of spinal dysraphism first described as a clinical entity by Pang et al. [1] in which disjunction of the surface- and neuroectoderm is unsuccessful and consequently causes incomplete closure of the neural tube. We have previously reported on a similar lesion in 2008, deemed *the dermal-sinus-like stalk*, which can be recognized as a form of LDM [2]. In

LDM, nondisjunction of the ectodermal layers ultimately results in the formation of a fibroneural stalk [3]. Together with a saccular or nonsaccular focal midline skin defect, these clinical entities are regarded as the hallmark of LDM [1, 4]. In saccular LDM, a skin-based cerebrospinal fluid (CSF) sac is topped by a squamous epithelial dome whereas in nonsaccular or flat LDM, the epithelial skin lesion is flat, sunken or contains a crater or pit [5]. Even though the presence of neuroglial tissue in the stalk is considered a central feature of LDM, several reports have indicated that the “neuronal” aspect cannot always be determined [5–8]. Here, we report a rare case of membranous LDM in which the histological presence of neuroglial tissue in the resected stalk could not be demonstrated.

## Case Description

A 27-year-old primigravida was referred to our center after ultrasound examination a 12 gestation revealed a lumbosacral CSF filled lesion. Consequently, at 17 weeks of gestation, antenatal magnetic resonance imaging (MRI) was performed to further ex-



**Fig. 1.** **a–c** Prenatal MRI at 17 weeks of gestation. **a** Sagittal T<sub>2</sub>-weighted MR image shows a lumbar spinal defect with a cystic component (arrow). No Chiari malformation or other defects are present. **b** Transversal T<sub>2</sub>-weighted MR image of the spine. The 2.6 × 3.2 mm cystic lesion (asterisk) is depicted and seems to contain a stalk. **c** Transversal T<sub>2</sub>-weighted MR image illustrates a stalked connection between the cystic lesion and the dura (arrow). **d–f** Two-day postnatal MRI. **d** Sagittal view illustrates a lesion at the

L4-L5 level with tenting of the dura. Furthermore, there is a stalked connection (arrow) between the dura and the cystic lesion (asterisks). **e** Transversal MR image shows the stalked connection (arrow) between the cystic lesion (asterisks) and the dura. **f** Transversal MR image depicts the cystic lesion (asterisks). The conus (arrow) shows a cystic dilatation of the central canal giving rise to a horseshoe-like configuration on the posterior side and is continuous with the stalk.

amine the defect. The observed fluid-filled mass (2.6 × 3.2 mm) contained a fistula connecting to a cystic component and was described as a “stalked” meningocele (Fig. 1a–c). There were no other defects present. Additionally, a second MRI 1.5 months later revealed the previously described defect to be unchanged.

The mother was induced into labor at 38 weeks and 4 days of gestation and delivered a healthy male infant weighing 3,200 g by vaginal parturition. The infant had a good start with Apgar scores of 9 and 10 after 1 and 5 min, respectively. Physical examination revealed a lumbosacral stalked lesion of 1 cm with a membranous sac of approximately 5 cm (Fig. 2). No neurological abnormalities were present. Because the cystic sac spontaneously ruptured the following day, the defect was sterilely dressed and amoxicillin/ceftazidime was administered to prevent infectious complications. Two-day postnatal MRI confirmed a defect at the level of L4-L5 with tenting of the dura and a dural sleeve that seemed to be connected to the cystic lesion (Fig. 1d–f). Since no cauda fibers were observed entering the sac on both MRI and ultrasound imagery, a meningocele was suspected, opposed to a myelomeningocele. Three days postpartum, the suspected meningocele and stalk were surgically resected under intraoperative neurophysiological monitoring. Recordings were obtained from the lower leg muscles (m. quadriceps femoris, m. tibialis anterior, and m. gastrocnemius) and the external anal sphincter.

Dissection along the stalk was performed to reveal a defected L4 and incompletely formed L5 vertebral arch. Laminectomy at L4 and flavectomy at L3-L4 showed a normal appearing dura. The dura was opened sharply, and the conus was observed. The stalk was continuous with the dorsal part of the conus, whereas the ventral part of the conus was connected to the atypically thick and nonelastic filum (Fig. 3). Stimulation of the proximal side (closer to the spinal cord) of the stalk registered during intraoperative neurophysiological monitoring and correspondingly some small nerve roots were observed. Thereupon, the stalk was resected just distally of this region and sent in for histopathological review. The filum was sectioned to untether the cord after which duraplasty followed. Apart from delayed wound-healing for which the patient was observed, postoperative recovery was uncomplicated, and no neurological deficits were observed.

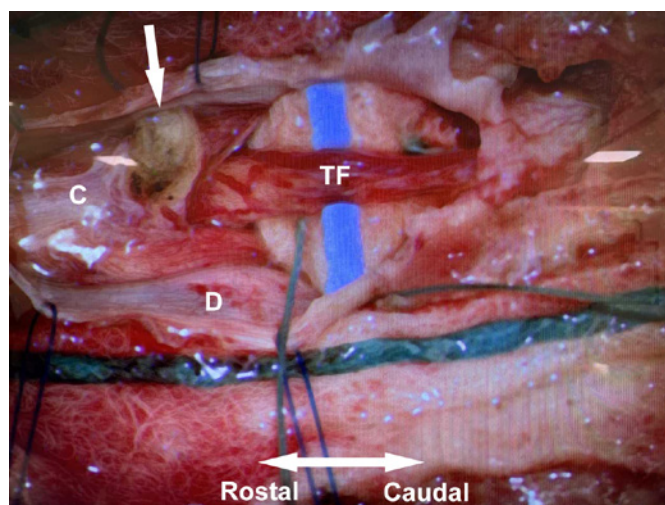
Histopathological examination of the stalk revealed lipid and collagenous connective tissue outlined by stratified squamous epithelium (Fig. 4c). S-100 immunostaining (DAKO GA504) revealed numerous peripheral nerve fibers, however, no central nervous tissue was found in the tract (Fig. 4a, b). The histopathology of the sack-wall revealed fibrous tissue outlined by cuboid and flattened epithelium (Fig. 5), which is suggestive for meningeal tissue.

## Discussion

In the present study, we report on a case of membranous LDM in which neuroglial tissue could not be demonstrated histologically. The current paradigm indicates that LDM arises from a sequential incomplete fusion followed by nondisjunction of the cutaneous- and neural-ectoderm, which ultimately results in a dorsal median tract of neuroectodermal tissue linking the focally incom-



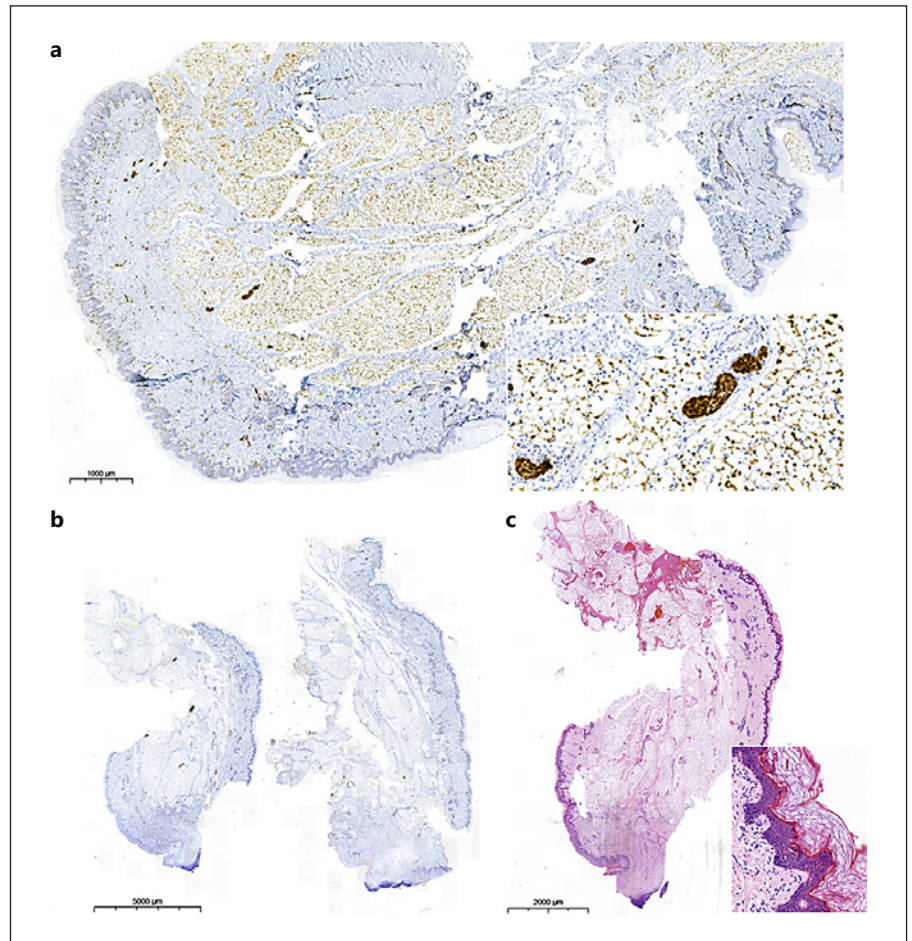
**Fig. 2.** Male neonate with a saccular dorsal midline lesion and membranous sac.



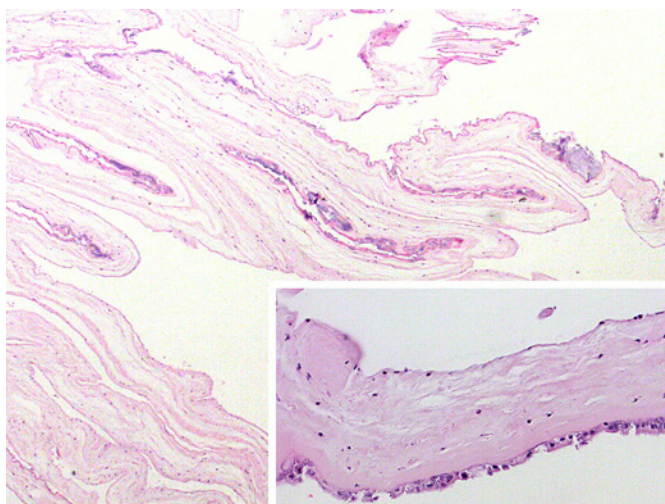
**Fig. 3.** Resection of the stalk reveals its attachment (arrow) to the conus (C). Furthermore, an atypically thick filum (TF) is noted. D, dura.

plete neural tube and the closed surface ectoderm [3]. Mesenchymal condensation along the neuroglial stalk explains the presence of mesodermal derived tissues [3]. This indicates, that along the stalk, neuroglial tissue should be observed [1, 4].

Since neurological complications in LDM arise due to tethering of the cord, performing a more distal resection of the stalk for the sake of histological confirmation of neuroglial tissue does not seem to weight up to the risks that accompany a more radical exposure and distal ligation of the stalk [6, 9]. Correspondingly, in our case, some



**Fig. 4.** Histopathological overview of the stalk. **a** S-100 staining (DAKO GA504) highlighting numerous peripheral nerves. **b** GFAP staining (DAKO IR524) shows no immunopositive glial tissue is present. **c** HE stained coupe in which mostly adipose and dermal tissue is present, outlined by stratified squamous epithelium. GFAP, glial fibrillary acidic protein.



**Fig. 5.** Histopathological overview of the membranous sac under HE-staining. The membranous sac contains fibrous tissue outlined by cuboidal and flattened epithelium.

small nerve roots were observed running along the more proximal part of the stalk, and thus, we resected the stalk just distally from that point to prevent neurological complications. Therefore, we cannot exclude the possibility that the more proximal unresected part of the stalk did contain neuroglial tissue.

The peripheral nerve fibers observed in our case have been hypothesized to arise from the entrapment of neural crest cells in the developing stalk [1]. While peripheral nerve fibers were present in all stalks in the original case series by Pang et al. [1], they have also been identified in cases of LDM where neuroglial tissue could not be demonstrated histologically [8]. In these cases, the presence of peripheral nerves under S-100 might serve as an additional histopathological finding to support the diagnosis of LDM [3, 5, 8].

Remarkably, histopathological examination additionally revealed a squamous epithelial lining of the tract. While ectopic squamous epithelium [5] and mixed le-

sions [3, 10] have been readily described in LDM, an epithelial lining is more typically observed in congenital dermal sinus. Given the absence of (epi-)dermoid tumors, a sinus tract, or clinical signs of infection along with observed tenting of the dura and the intradural attachment of the stalk, we believe that a congenital dermal sinus is highly unlikely in this case [11].

Much like our case, several reports have indicated that the neuronal aspect in LDM cannot always be demonstrated histologically [5–8]. In the case series of Morioka et al. [5], two out of 4 cases of nonsaccular LDM did not show glial fibrillary acidic protein-immunopositive neuroglial tissue. In succession of their first paper, Morioka et al. [8] (re-)examined almost the entire tract of five out of 6 patients with nonsaccular LDM. Despite their relatively extensive histopathological examination, only 50% contained glial fibrillary acidic protein-immunopositive neuroglial tissue with no neuroglial tissue being observed in most and the main part of the stalk [8]. Furthermore, reports by Lee et al. [6] ( $n = 9$ ) and Kim et al. [7] ( $n = 23$ ) both describe cases of “probable” LDM in which histopathological determination of CNS is not possible in the resected part of the stalk. Collectively, they conclude that the neural component is likely to be present in the unresected portion of the stalk [6, 7]. However, the obvious alternative explanation of neuroglial tissue simply being absent should at least be entertained.

During neural tube development, delamination of the cutaneous- and neuroectoderm occurs by the formation extracellular matrix, resulting in an inter-epithelial space between the separating ectodermal layers [12]. As fusion of the neural tube proceeds, the inter-epithelial spaces coalesce and final disjunction of the cutaneous- and neuroectoderm is completed. Subsequent paraxial mesoderm migration occurs in the inter-epithelial space to ultimately form the dorsal vertebral structures. Interestingly, defective mesodermal cell migration has readily been described as a mechanism for spina bifida, given that paraxial mesoderm plays a key role in the coordination of neural tube closure [13].

Although neural tube defects have often been attributed to the primary failure of neural tube closure, there is a compelling body of both clinical and experimental work suggesting secondary opening of the neural tube as a mechanism for neural tube defects [14, 15]. Among theories, it has been proposed that the hydrostatic pressure of secreted neural tube fluid can cause subsequent rupture of the neural tube [16]. We believe that secondary reopening of the neural tube forms a possible mechanism by which mesodermal tissue can invade the neural tube and

cause the focal connection between the neuro- and cutaneous ectoderm. Elongation of this mesodermal strand can lead to the formation of a mesenchymal stalk without a lumen and without the presence of neuroglial tissue. Additionally, the saccular aspect can be explained by the largely undifferentiated mesodermal tissue being subjected to hydrodynamic CSF pressure, ultimately leading to the formation of a membranous sac. Although the histopathology of the membranous sac was suggestive for meningeal tissue, it remains difficult for us to place meningeal development in the currently leading theory of LDM or our proposed alternative. Given that the current knowledge regarding spinal meningeal formation is limited and controversial [17, 18], we believe this forms an important area for further research.

## Conclusion

If anything, the current paper highlights that the pathoembryogenesis of spinal dysraphisms are poorly understood. Given the absence of a clear and experimentally substantiated pathoembryological theory, it is difficult to give this form of spinal dysraphism a name linked to its embryological origins, such as LDM. Furthermore, it excludes the possibility of other possible mechanisms, as described in this paper, by which this form of spinal dysraphism can arise. Therefore, we believe that the term neural tube disorder, as previously proposed by others [14, 15], more accurately encompasses the known etiology of the disease while simultaneously leaving room for further research to draw more substantiated conclusions on its embryological origins.

## Statement of Ethics

Written informed consent was obtained from the parents of the patient for publication of this case report and any accompanying images. Ethical approval was not required for this study in accordance with national guidelines.

## Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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## Author Contributions

Casper Vrij and Tim Bouwens van der Vlis drafted the manuscript. Maud Tijssen, Jan Beckervordersandforth, and Jasper van Aalst were all involved in the clinical care of the patient and revised the manuscript.

## Data Availability Statement

All data generated or analyzed during this study are included in this article. Further enquiries can be directed to the corresponding author.

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