

**TITLE: Management of an unusual, recurrent neurenteric cyst in an infant: case report and review of the literature**

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**RUNNING HEAD**

Recurrent Spinal Neurenteric Cyst

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## **Abstract**

Neurenteric cysts are rare congenital remnants formed by a failure of separation between endoderm and ectoderm in utero. We describe a case of a 7-month-old male with a large cervical neurenteric cyst presenting with intermittent neck stiffness and irritability. This cyst was resected, recurred, and required repeat surgery. The patient's postoperative course included aseptic meningitis and hydrocephalus requiring ventriculoperitoneal shunt, and later management of tethered cord, necessitating detethering. Unique features of this case include the presence of intermittent pain symptoms, which may be attributable to cyst filling and emptying. Hydrocephalus is an uncommon finding that may be secondary to aseptic meningitis from cyst rupture. Tethered cord is also an unusual entity that can accompany this diagnosis, warranting additional imaging workup and monitoring.

## **Keywords**

Aseptic Meningitis, Congenital, Enterogenous Cyst, Hydrocephalus, Neurenteric Cyst, Tethered Cord

## **Introduction**

Neurenteric cysts are rare, benign lesions that make up anywhere from 0.3[1] to 1.3%[2] of spinal tumors. Neurenteric cysts are congenital remnants formed from an anomalous connection between the endoderm and ectoderm during the third week of life, leading to a persistent endoderm in the spinal canal with occasional connection between the spinal canal, gut, or skin[3-5].

These lesions, although rare, usually manifest in adults, and are associated with vertebral abnormalities[6]. In the pediatric population, they show a male predominance, with a mean age of 5 years on presentation[7, 8]. Neurenteric cysts are space-occupying and can compress neural structures, presenting with progressive pain, myelopathy, and radiculopathy[7]. Rarely, these lesions present with fluctuating symptoms attributed to changing cyst volume or location[9], and concurrent neurologic conditions, like tethered cord[10, 11].

In this report we describe an unusual case of a 7-month-old male infant with a large, cervical neurenteric cyst presenting with fluctuating symptoms that underwent resection, recurred, and subsequently developed hydrocephalus and tethered cord. We discuss the unique presentation, indications for surgery, common complications, and neurosurgical comorbidities of this rare diagnosis.

## **Case Report**

### *History and Imaging*

A 7-month-old male infant was admitted to the hospital with episodic neck and extremity stiffness. He previously had two emergency room visits, and was diagnosed with otitis media on one instance and constipation on the second. On the third presentation, his neck stiffness was evaluated with a cervical MRI which revealed a dorsal, 5.5x1.5cm non-enhancing lesion isointense to cerebrospinal fluid (Fig 1). Mass effect and rightward displacement of the cervical spinal cord was noted, and a preliminary diagnosis of arachnoid cyst was established. MR imaging of the lumbar spine demonstrated filum lipoma, which was observed with surgical management planned for a future date. Remaining imaging of the spine and brain was unremarkable, with normal ventricular size. CT imaging revealed expected incomplete fusion of the arches of C1 and C2, but was otherwise unremarkable.

On examination the patient's episodic pain had resolved, was found to be calm and appropriate, with intact strength, sensation, normal reflexes, and no myelopathic signs. A strawberry hemangioma were noted overlying the cervical spine just left of midline. The patient's medical, birth, and family history were otherwise unremarkable.

### *First Operation*

An initial diagnosis of arachnoid cyst was established, and the patient planned for laminectomy, cyst debulking, and fenestration. The patient underwent C1 arch removal with partial C2 laminectomy several days later. On dural opening a white, fibrous membrane was observed inflating and deflating with fluid in an oscillating fashion. This membrane was fenestrated and a wispy, milky fluid was evacuated under pressure. Given the unusual appearance of cyst

contents, a different pathology was suspected and the cyst wall was partially resected. Given the limited cervical exposure, caudal portions of the cyst wall adherent to the underlying spinal cord were left in situ. The dura was then closed in a watertight manner.

Postoperatively the patient had resolution of his episodic pain and stiffness, with repeat MRI showing partial decompression of the cyst and spinal cord (Fig 2). Pathology returned periodic acid-Schiff (PAS)-positive mucin producing cells which were positive for cytokeratin and negative for glial fibrillary acidic protein (GFAP), and a diagnosis of Wilkins and Odum Type A[12] neurenteric cyst was established (Fig 3).

#### *Cyst Recurrence and Second Operation*

The patient returned at 15 months of age with similar symptoms of irritability and stiffness of the neck and extremities. Repeat MRI (Fig 4a) revealed recurrence of the lesion, and, with diagnosis of neurenteric cyst established, gross total resection was planned. The patient returned to the operating room for C3, 4, and partial C5 laminectomy. Care was taken to remove the cyst en bloc, however, the cyst was inadvertently ruptured on dural opening. Cottonoids were applied to minimize introduction of cyst contents into the CSF space. The cyst was found attached to the dura on the anterior aspect of the spinal canal, gently mobilized, and systematically resected. A small piece adhered to the spinal cord and nerve roots was left in place and cauterized with bipolar cautery.

Postoperative imaging revealed cyst resection with a small pseudomeningocele (Fig 4b). The patient was readmitted a week later with high fever and lumbar puncture suggestive of aseptic meningitis. When repeat MRI showed growth of the pseudomeningocele, the patient returned to the OR for CSF leak repair and lumbar drain placement with subsequent improvement.

#### *Hydrocephalus and Tethered Cord*

At 17 months of age, the patient returned with irritability. While repeat cervical imaging revealed pseudomeningocele resolution, MRI of the brain displayed increased ventricular size and transependymal flow suggestive of hydrocephalus (Fig 5a). The patient subsequently underwent ventriculostomy, and following negative CSF cultures, ventriculoperitoneal shunt placement with resolution of symptoms.

Lumbar MR imaging throughout the patient's life was significant for fatty filum terminale and low lying conus (Fig 5b), with normal neurologic and urologic function. Surgery was deferred until the patient was 4 years of age, after which the patient underwent elective lumbar laminectomy, cord detethering, and fatty filum resection without complication. At the patient's last visit at 7 years of age, the patient was in second grade, ambulatory, and without evidence of cyst recurrence.

## Discussion

### *Presentation and Classification of Neurenteric Cysts*

Spinal neurenteric cysts are developmental abnormalities that go by many names, including enterogenous cysts, endodermal cysts, dorsal enteric fistulas, and split notochord syndrome[4]. Neurenteric cysts are rare, presenting in adults in the second and third decades of life, with a 2:1 male predominance[13], and are most frequent in the cervicothoracic region[7, 8]. In children they are most common around 5 years of age, although they have been reported in infants as well[7]. Neurenteric cysts typically present with gradual onset of pain, paraplegia or myelopathic signs, which can be attributed to mass effect from the cyst itself. Unlike most spinal tumors, however, symptoms sometimes fluctuate in intensity, as was the case in this patient, a unique feature attributable to the alternating filling and emptying of cyst contents[9, 14].

On imaging, neurenteric cysts are nonenhancing, T1 hypo or isointense, T2 hyperintense, and appear similar to arachnoid cysts, which was the preoperative diagnosis in this patient. Unlike arachnoid cysts, however, neurenteric cysts tend to be more ventrally located and isointense on T1 from proteinaceous cyst contents[15]. They are associated with both bony and cutaneous abnormalities, most commonly Klippel-Feil, which have been reported in both small[16] and large[6] percentages of patients across various studies. Neurenteric cysts are considered to arise from splitting of the notochord during the third week of gestation[6], allowing for endoderm to herniate through the developing spine and communicate with overlying ectoderm. Histologically, the endoderm origin of neurenteric cysts gives them a gastrointestinal or respiratory appearance, with cuboidal, columnar, or ciliated cells positive on PAS and cytokeratin stains[12], which

helps differentiate them from the menigothelial structure of arachnoid cysts.

Many theories exist to account for the presence of neurenteric cysts. The Pang classification[17] proposes that in patients with split cord malformations, an accessory neurenteric canal bisects the developing notochord and can result in a number of remnants including dorsal tethering, myelomeningocele, and neurenteric cysts. The Bentley and Smith classification[3] (Fig 6), first proposed in 1960, categorizes congenital posterior enteric remnants, ranging from complete fistula from gastrointestinal tract to skin (Type I) through an enteric diverticulum communicating with the GI tract alone (Type IV). Most neurenteric cysts, including this case, fall under this classification as isolated lesions that communicate neither with the skin nor GI tract, and include subcutaneous, intradural-extramedullary, and intramedullary subtypes (Type III).

#### *Cyst Recurrence*

Gross total resection is optimal in the treatment of neurenteric cysts, and is generally curative[8]. This is not always possible, however, in patients with ventral or intramedullary lesions, as well as cysts that adhere to the spinal cord or nerve roots[18, 19], such as the patient in this report. Previous studies have reported rates of recurrence ranging from 11%[19] to 63%[18] in patients with subtotal resection, with most patients presenting again within a few years. Repeat surgery in patients with recurrent cysts, however, can have excellent outcomes. Consequently, the surgeon must weigh carefully the benefit of goal of total resection versus debulking alone to avoid neurologic deficits.

#### *Hydrocephalus and Tethered Cord*

Delayed hydrocephalus is a rare presentation in patients with neurenteric cysts[20]. A plausible hypothesis for this finding is the development of aseptic meningitis from leakage of cyst contents or intraoperative cyst rupture[1, 7]. Aseptic meningitis is uncommon in neurenteric cysts because mucin, produced from cyst endodermal lining, is usually not harmful to the leptomeninges. Sometimes, however, high cytokeratin content or other debris in the CSF may induce arachnoid inflammation and cause hydrocephalus by blocking absorption mechanisms[21]. In this case, cyst contents, which leaked during both operations, likely had a high concentration of cytokeratin. This, along with debris from multiple surgeries, likely contributed to the development of fever and lumbar puncture suggestive of aseptic meningitis. Although not always

possible in patients with cysts adherent to neural structures, it is beneficial for cyst resection to be performed en bloc without violation of the capsule.

Tethered cord syndrome and filum lipoma are uncommon, but have been associated with neurenteric cysts in a few studies[6, 10, 11]. Detethering is indicated in patients with urologic or neurologic deficits. Symptoms in tethered cord are considered to be secondary to decreased blood flow and mitochondrial activity from progressive stretch of the relatively inelastic caudal cord, leading to impaired oxidative metabolism and ischemia[22]. Although case reports with neurenteric cysts are few, cysts may contribute to worse symptoms by applying additional mass effect on the caudal spinal cord, particularly in intramedullary and lumbar lesions[10].

#### *Special Considerations for the Neurenteric Cyst Patient*

Neurenteric cysts, although rare, are a distinct pathologic identity that should remain on the differential of the pediatric neurosurgeon. We recommend special consideration be provided in infants who present with intermittent episodes of neck stiffness and irritability, an unusual presentation seen in this patient, and largely unique among spinal tumors. Care should also be taken to identify cutaneous stigmata of an underlying lesion, myelomeningocele, or cutaneous fistula. If an underlying lesion is suspected, imaging should be performed and the radiologic features differentiating neurenteric from arachnoid cysts considered. Workup should also include complete neuraxis imaging to assess for other forms of spinal dysraphism, filum lipoma, and tethered cord. Once diagnosed, complete resection is preferable. Intraoperatively, care should be taken to avoid spillage of cyst contents which place the patient at risk of aseptic meningitis and hydrocephalus.

#### **Disclosure**

On behalf of all authors, the corresponding author states that there is no conflict of interest.

## Figure Legends

**Fig 1** MR imaging on presentation at 7 months. A large dorsal 5.5x1.5cm non-enhancing lesion was noted extending from the C1 to C6 levels (**A**). On axial imaging, rightward displacement of the cervical cord (**B**) was observed

**Fig 2** Postoperative MRI. After C1 arch resection and partial C2 laminectomy, the cyst was debulked with decompression of the cyst and underlying spinal cord (**A**). Some mass effect persisted after the operation, best appreciated on axial view (**B**)

**Fig 3** Micrographic images of resected neurenteric cyst wall. Mucin-producing columnar cells are visible, mimicking gastrointestinal epithelium. H&E, original magnification x100

**Fig 4** Cyst recurrence and resection. 8 months after the initial operation the patient had recurrence of symptoms and imaging revealed cyst recurrence (**A**). Postoperatively the patient developed pseudomeningocele (**B**) requiring CSF leak repair and lumbar drain placement

**Fig 5** Hydrocephalus and tethered cord. Two months after recurrence of the neurenteric cyst and repeat resection, the patient developed hydrocephalus (**A**) requiring ventriculoperitoneal shunting. Lumbar imaging throughout the patient's life was suggestive of cord tethering and fatty filum (**B**), for which the patient underwent detethering at 4 years of age

**Fig 6** Bentley and Smith classification[3] of congenital posterior enteric remnants. This patient presented with an intradural, extramedullary dorsal enteric (neurenteric) cyst (Type III)



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