## Case Report

# Spinal endodermal cyst resembling an arachnoid cyst in appearance: Pitfalls in intraoperative diagnosis of cystic lesions

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## Abstract

**Background:** Surgical treatment of endodermal cysts requires total removal of the cyst wall during the first operation to prevent recurrence. Therefore, intraoperative pathological diagnosis plays an important role in determining the optimal surgical strategy. We present a rare case of a spinal endodermal cyst and discuss its diagnostic difficulty during the intraoperative pathological examination.

**Case Description:** An 18-year-old male presented with progressive paraparesis and precordial oppression. Magnetic resonance (MR) imaging revealed an intradural extramedullary cystic mass having the same signal intensity as cerebrospinal fluid (CSF) without gadolinium enhancement at the T1-T2 level. The preoperative diagnosis was an endodermal or arachnoid cyst. The patient underwent surgery. An intraoperative frozen section showed a cyst wall consisting of loose, thin, fibrous tissue intermittently covered by flattened epithelium. The diagnosis was an arachnoid cyst. Accordingly, partial resection of the cyst wall was performed to create CSF communication between the cyst and subarachnoid space. However, the postoperative pathological diagnosis from permanent sections was an endodermal cyst, which was lined with ciliated columnar epithelium that was immunopositive for cytokeratin and epithelial membrane antigen. Subsequent paraffin embedding and immunostaining of the intraoperative frozen sample also confirmed patchy cytokeratin expression by all flattened epithelial cells. The patient's cyst had refilled 10 months after surgery, and he subsequently underwent fenestration of the cyst wall and placement of a cyst-subarachnoid shunt.

**Conclusion:** Examination of multiple samples from multiple sites or intraoperative immunostaining of frozen sections is recommended for accurate intraoperative diagnosis of endodermal cysts.

**Key Words:** Intradural spinal cyst, endodermal cyst, arachnoid cyst, intraoperative pathological diagnosis, cytokeratin

## INTRODUCTION

Endodermal cysts are rare, but well-known cystic lesions of the spinal canal that occur in the lower cervical and upper thoracic spine in particular.[15] Despite their benign nature, cysts recur in the residual lesion. To prevent recurrence, it is necessary to remove as much of the lesion as possible.[4] Therefore, intraoperative pathological diagnosis has an important impact on the choice of procedures and the extent of surgery.

We report here a case of a spinal endodermal cyst that was diagnosed intraoperatively as an arachnoid cyst. We demonstrate detailed clinicopathological findings and discuss the difficulty in pre- and intraoperative diagnosis of spinal cystic lesions.

## CASE REPORT

An 18-year-old male presented with a 1-month history of progressive weakness in the lower extremities and progressive precordial oppression. He had a three-year history of occasional precordial oppression. Neurological examination revealed mild symmetric paraparesis with grade 4+/5 strength on manual muscle testing and bilateral severe hypesthesia below the T4 level. The deep tendon reflex in the lower extremities was markedly increased, and Babinski's sign was observed bilaterally. He had difficulty with tandem gait. His peak urinary flow rate was moderately decreased. Magnetic resonance (MR) imaging of the thoracic spine revealed an intradural extramedullary cystic tumor at the T1-T2 level that was severely compressing the spinal cord from the ventral side [Figure 1]. The contents of the cyst showed signal intensity nearly identical to that of the cerebrospinal fluid (CSF) on T1- and T2-weighted MR images [Figure 1]. The tumor showed no enhancement on gadolinium-enhanced T1-weighted MR images. There were no other abnormal findings including vertebral body anomalies, spina bifida, or a mediastinal mass.

Tumor removal was performed through a C7-T2 laminoplastic laminotomy. The spinal cord was bulging, but the cyst wall was not identified through the pia mater. After the spinal cord was longitudinally split along the posterior median sulcus, the cyst wall, which had a thin, translucent, membranous appearance, was identified at the ventral side of the flattened spinal cord through the split posterior median sulcus [Figure 2a]. The cyst was aspirated with a 24-gauge elastic needle [Figure 2a]. The contents of the cyst consisted of a serous, clear, and colorless fluid similar to the CSF. The cyst wall was tightly attached to the spinal cord, and was peeled off as much as possible. The intraoperative pathological diagnosis with frozen sections was an arachnoid cyst [Figure 2b and c, see below for details]. Therefore, further resection of the tumor was not performed to avoid damage to the spinal cord. The ventral part of the cyst wall was opened to allow the CSF to flow freely. There were no somatosensory or motor-evoked potential changes in the lower extremities during the operation. Postoperative MR imaging demonstrated marked shrinkage of the cyst [Figure 3a]. The patient experienced no postoperative complications, and all symptoms including precordial oppression, decreased peak urinary flow rate, sensory abnormalities, and mild paraparesis disappeared. However, 10 months after surgery, the patient noted precordial oppression again, and MR imaging revealed that the cyst had refilled [Figure 3b].

Eleven months after the first operation, fenestration of the cyst wall and insertion of a cyst-subarachnoid shunt were performed using the same approach as the first operation [Figure 3d]. Because the cyst wall was found to have adhered tightly to the spinal cord during the first operation, we chose continuous drainage of the cyst fluid into the subarachnoid space using a cyst-subarachnoid shunt in the second operation rather than resection of the cyst wall to prevent spinal cord damage. The contents of the cyst were again similar to that of the CSF [Figure 3c], and contained 18 mg/dl protein, <1 mg/dl glucose, 153 mmol/l sodium, 3.0 mmol/l potassium, and 135 mmol/l chlorine. One end of the shunt tube was inserted into the cyst through the split posterior median sulcus, and the other end was placed in the dorsal subarachnoid space of the spinal cord [Figure 3d]. After the operation, precordial oppression disappeared. He was discharged with no neurological deficits.

## PATHOLOGICAL FINDINGS

Intraoperative pathological examination of frozen sections revealed that the cyst wall was composed of a loose, thin, fibrous membrane containing melanocytes and was intermittently lined with flattened or partially cuboidal epithelial cells [Figure 2b and c]. No ciliated cells or mucin-producing cells were detected in the epithelium. Because the features were suggestive of the arachnoid membrane, the cyst was diagnosed as an arachnoid cyst. However, permanent paraffin sections revealed that the cyst wall was composed of a thin, fibrocollagenous tissue lined with ciliated columnar epithelial cells and mucin-producing cells [Figure 4a and b]. Immunohistochemistry on permanent paraffin sections revealed that the epithelial cells were positive for cytokeratin (CAM5.2, Figure 4c; AE1/AE3, data not shown) and epithelial membrane antigen, but negative for glial fibrillary acidic protein (data not shown) and S-100 protein [Figure 4e], ruling out a glial origin of the epithelium. Some of the epithelial cells were immunopositive for Ki-67 (data not shown). Periodic acid-Schiff staining revealed mucin production in a population of the epithelial cells [Figure 4d]. The final pathological diagnosis was thus
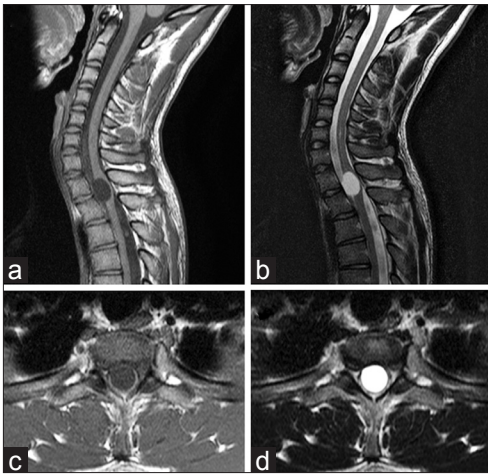
**Figure 1: Preoperative T1-weighted (a, c) and T2-weighted (b, d) magnetic resonance images without gadolinium enhancement demonstrating an intradural extramedullary cystic tumor at the T1-T2 level. (a, b) Sagittal view and (c, d) axial view**
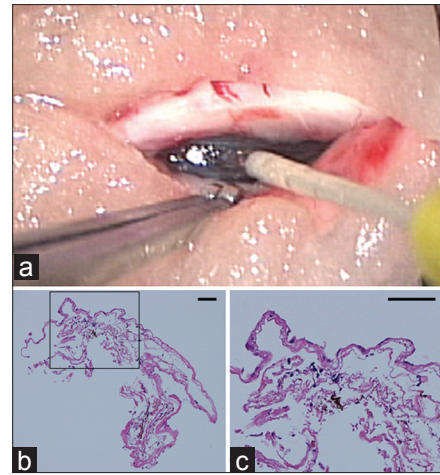


**Figure 2: (a) Intraoperative photograph of the cyst wall. (b, c) Paraffin section of the intraoperative frozen sample (H–E staining; scale bars represent 50 µm); (b) a magnified view of the region in the square in panel (c)**
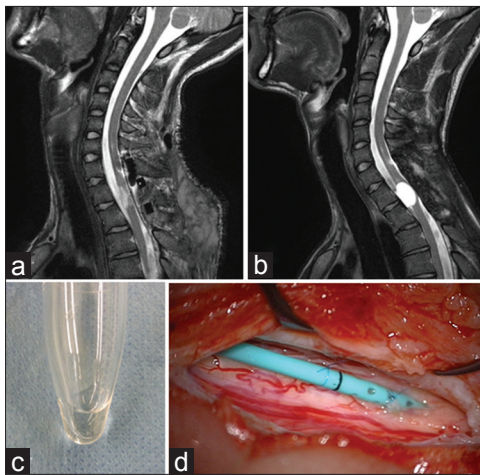


**Figure 3: (a, b) T2-weighted magnetic resonance images at 1 day (a) and 10 months (b) after the first surgery. (c) Contents of the cyst. (d) Intraoperative photograph of the second operation showing a cyst-subarachnoid shunt tube inserted into the cyst**
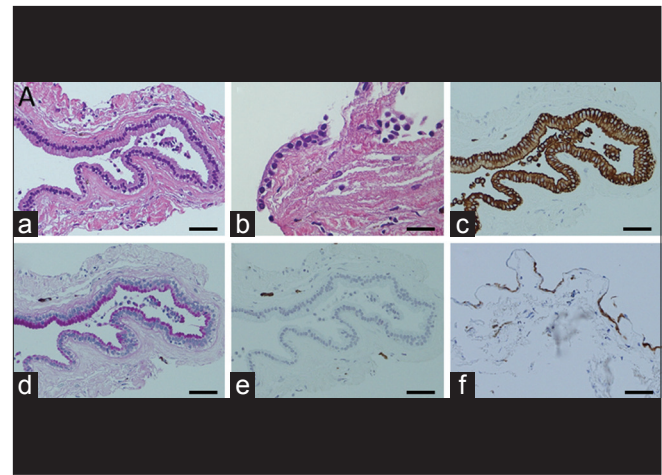


**Figure 4: Histopathological findings on permanent paraffin sections (a–e) and a paraffin section prepared from the remaining frozen sample (f) (scale bars represent 50 µm except (b); 30 µm). (a, b) H–E staining. (c, f) CAM5.2. (e) S-100 protein. (d) PAS staining**

an endodermal cyst. Because there was a discrepancy in the histological findings between the intraoperative frozen sections and the permanent paraffin sections, immunohistochemistry was performed on the frozen samples that were subsequently subjected to paraffin embedding as a frozen control. This staining revealed that the flattened epithelial cells were immunopositive for the cytokeratin antibodies CAM5.2 [Figure 4f] and AE1/AE3 (data not shown). The immunophenotype was thus similar to that of the epithelial cells in the permanent specimen.

## DISCUSSION

Endodermal cysts occur most frequently in the spinal canal, mainly in the lower cervical and upper thoracic

spine.[15] The typical presentation is an intradural and extramedullary cystic mass compressing the spinal cord from the ventral aspect, similar to what was seen in the present case.[3]

Endodermal cysts are usually iso- to hypointense on T1-weighted MR images, iso- to hyperintense on T2-weighted MR images, and show no restriction of water diffusion on diffusion-weighted (DW) MR images.[11,19] In general, the absence of contrast enhancement of the cyst wall with gadolinium is useful for distinguishing endodermal cysts from other cystic lesions such as cystic schwannomas,[10] cystic meningiomas,[2] cystic ependymomas,[8] and cysticercosis.[1,16] Differential diagnosis of spinal intradural nonenhanced cystic lesions mainly includes endodermal cysts, arachnoid cysts,

epidermoid cysts, and dermoid cysts.[17,24] Arachnoid cysts are isointense relative to the CSF on MR images obtained with all sequences. Therefore, their differentiation from endodermal cysts is difficult when endodermal cysts have the same signal intensity as the CSF.[22] Epidermoid cysts are usually isointense relative to the CSF on both T1- and T2-weighted MR images, but show restriction of water diffusion on DW images. Dermoid cysts show heterogeneous signal intensity on both T1- and T2-weighted MR images and restriction of water diffusion on DW images.

Considering the location and radiographic appearance of the lesion and the progressive clinical course of our patient, the cyst was preoperatively diagnosed as an endodermal cyst in the present case. However, the signal pattern of the cyst fluid was similar to the CSF on MR images, and so preoperatively, we could not completely rule out a spinal intradural arachnoid cyst. The therapeutic strategy for endodermal cysts is different from that for arachnoid cysts. For endodermal cysts, recurrence is frequent when the lesion is not completely removed. Total removal of the cyst wall is therefore recommended during the first surgery.[23] In contrast, total removal of the cyst wall is unnecessary with arachnoid cysts. Cyst excision or fenestration into the subarachnoid space is sufficient, because the aim of surgical treatment is to create communication of the CSF between the cyst and the adjacent subarachnoid space.[9,21] Therefore, intraoperative diagnosis is crucial for selecting an appropriate surgical strategy.

In the present case, there was a discrepancy in the diagnosis between frozen sections and permanent paraffin sections. The findings in the intraoperative frozen specimen suggested an arachnoid membrane with mechanically deformed arachnoid cells due to the pressure of the cyst contents rather than an endodermal cyst because the cyst wall was composed of flattened epithelial cells with neither cilia nor discernible mucin production intermittently lining a loose, thin, fibrous tissue containing melanocytes. In addition, macroscopic observation during the operation also revealed that the cyst wall consisted of a thin, whitish, translucent membrane that was similar to the arachnoid membrane, and the cyst fluid was similar in appearance to the CSF. According to the intraoperative diagnosis, we performed a partial resection of the cyst wall to create communication between the cyst and the subarachnoid space. Subsequent paraffin embedding and immunohistochemistry of the intraoperative frozen sample confirmed that the epithelium was immunopositive for cytokeratin.

In general, cytokeratins are expressed specifically in epithelial cells. It has been reported that normal arachnoid cells do not express cytokeratin.[12,18] On the other hand, Frank et al. have reported in vitro expression of cytokeratins in certain cultured cells believed to be derived from human arachnoid cells.[7] Kasper et al. reported that cytokeratin 8 and 18 are abundant in fetal arachnoid cells, and cytokeratin 8 is expressed in adult arachnoid cells. However, in adults, immunoreactivity is restricted to only a few cells.[13] Because both CAM5.2[25] and AE1/AE3[5] antibodies recognize cytokeratin 8, we cannot completely exclude the possibility of the presence of cytokeratin-positive arachnoid cells in our intraoperative sample. However, diffuse, strong immunoreactivity for cytokeratin in the intraoperative specimen suggests that epithelial cells in the frozen sample were derived from the cyst wall of an endodermal cyst rather than being arachnoid cells. It is possible that original columnar epithelial cells had been flattened and had detached from the basement membrane. Fortuna and Mercuri suggested that chronic intracystic pressure may cause changes in the original structure of intradural spinal cysts including arachnoid cysts, neuroepithelial cysts, and endodermal cysts.[6] In our case, long-term compression due to chronic, high intracystic pressure may have caused detachment and flattening of the epithelial cells as well as thinning of the connective tissue of the cyst wall.

For intraoperative frozen diagnosis of spinal cystic lesions, we recommend obtaining multiple frozen samples from multiple sites to help avoid misdiagnosis. In addition, rapid immunostaining of frozen sections within a tolerable time span during the operation is very helpful for obtaining an accurate diagnosis.[20] Krishnamurthy et al. reported the usefulness of rapid cytokeratin immunostaining on frozen sections for the intraoperative evaluation of metastasis of breast cancers in sentinel lymph nodes.[14] Their protocol for rapid immunostaining can be completed in 20–25 min, and it is likely feasible for intraoperative use.[14]

In the present case, the extent of the cyst removal could not have been increased even with a correct intraoperative diagnosis because of the tight adhesion of the cyst wall to the spinal cord tissue. However, additional procedures such as placement of a cyst-subarachnoid shunt would have been attempted at the initial surgery if the correct intraoperative diagnosis had been made based on appropriate sampling, and this may have prevented subsequent refilling of the cyst and reoperation. We conclude that it is important to recognize the above-mentioned pitfalls and the options for examining tissue for intraoperative diagnosis of cystic lesions.

## REFERENCES

1.  Bigner DD, McLendon RE, Bruner JM, editors. Russell and Rubinstein's Pathology of Tumors of the Nervous System. 6th ed. London: Hodder Headline Group; 1998.
2.  Chatzidakis EM, Volikas Z, Condilis N, Lypiridis S, Fratzoglou M, Simopoulos K. Spinal cystic meningioma presenting as a ring enhancing lesion on MRI. Ann Ital Chir 2008;79:197-8.

3. Chavda SV, Davies AM, Cassar-Pullicino VN. Enterogenous cysts of the central nervous system: a report of eight cases. Clin Radiol 1985;36:245-51.

4. Devkota UP, Lam JM, Ng H, Poon WS. An anterior intradural neurenteric cyst of the cervical spine: complete excision through central corpectomy approach--case report. Neurosurgery 1994;35:1150-3; discussion 1153-4.

5. Eichner R, Bonitz P, Sun TT. Classification of epidermal keratins according to their immunoreactivity, isoelectric point, and mode of expression. J Cell Biol 1984;98:1388-96.

6. Fortuna A, Mercuri S. Intradural spinal cysts. Acta Neurochir (Wien) 1983;68:289-314.

7. Frank EH, Burge BW, Liwnicz BH, Lotspeich LJ, White JC, Wechsler SL, *et al.* Cytokeratin provides a specific marker for human arachnoid cells grown *in vitro*. Exp Cell Res 1983;146:371-6.

8. Graca J, Gultasli N, D'Haene N, Brotchi J, Salmon I, Baleriaux D. Cystic extramedullary ependymoma. AJNR Am J Neuroradiol 2006;27:818-21.

9. Hanieh A, Simpson DA, North JB. Arachnoid cysts: A critical review of 41 cases. Childs Nerv Syst 1988;4:92-6.

10. Karatas A, Is M, Yildirim U, Akyuz F, Gezen F. Thoracic intradural cystic schwannoma: a case report. Turk Neurosurg 2007;17:193-6.

11. Karki P, Bohara M, Yonezawa H, Tokimura H, Hirano H, Hanaya R, *et al.* Cerebellopontine angle endodermal cyst presenting with hemifacial spasm. Brain Tumor Pathol 2011;28:371-4.

12. Kartenbeck J, Schwechheimer K, Moll R, Franke WW. Attachment of vimentin filaments to desmosomal plaques in human meningiomal cells and arachnoidal tissue. J Cell Biol 1984;98:1072-81.

13. Kasper M, Perry G, Stosiek P. Cytokeratin expression in human spinal meninges and ependymal cells. J Hirnforsch 1991;32:19-25.

14. Krishnamurthy S, Meric-Bernstam F, Lucci A, Hwang RF, Kuerer HM, Babiera G, *et al.* A prospective study comparing touch imprint cytology, frozen section analysis, and rapid cytokeratin immunostain for intraoperative evaluation of axillary sentinel lymph nodes in breast cancer. Cancer 2009;115:1555-62.

15. Lee SH, Dante SJ, Simeone FA, Curtis MT. Thoracic neurenteric cyst in an adult: case report. Neurosurgery 1999;45:1239-42; discussion 1242-33.

16. Leite CC, Jinkins JR, Escobar BE, Magalhaes AC, Gomes GC, Dib G, *et al.* MR imaging of intramedullary and intradural-extramedullary spinal cysticercosis. AJR Am J Roentgenol 1997;169:1713-7.

17. Lolge S, Chawla A, Shah J, Patkar D, Seth M. MRI of spinal intradural arachnoid cyst formation following tuberculous meningitis. Br J Radiol 2004;77:681-4.

18. Ng HK, Tse CC, Lo ST. Meningiomas and arachnoid cells: an immunohistochemical study of epithelial markers. Pathology 1987;19:253-7.

19. Preece MT, Osborn AG, Chin SS, Smirniotopoulos JG. Intracranial neurenteric cysts: imaging and pathology spectrum. AJNR Am J Neuroradiol 2006;27:1211-6.

20. Richter T, Nahrig J, Komminoth P, Kowolik J, Werner M. Protocol for ultrarapid immunostaining of frozen sections. J Clin Pathol 1999;52:461-3.

21. Schroeder HW, Gaab MR, Niendorf WR. Neuroendoscopic approach to arachnoid cysts. J Neurosurg 1996;85:293-8.

22. Shin JH, Byun BJ, Kim DW, Choi DL. Neurenteric cyst in the cerebellopontine angle with xanthogranulomatous changes: serial MR findings with pathologic correlation. AJNR Am J Neuroradiol 2002;23:663-5.

23. Wakao N, Imagama S, Ito Z, Ando K, Hirano K, Tauchi R, *et al.* A case of split notochord syndrome: an adult with a spinal endodermal cyst mimicking an intramedullary tumor. Neuropathology 2011;31:626-31.

24. Wilkins RH. Intraspinal cysts. In: Wilkins RH, Rengachary SS, editors. Neurosurgery. New York: McGraw-Hill; 1996.

25. Yao CC, Tseng SW, Han CP. Monoclonal antibody CAM5.2 can detect the cytokeratin 8, not cytokeratin 18. Comment on: "Occult disseminated tumor cells in lymph nodes of patients with gastric carcinoma. A critical appraisal of assessment and relevance. Langenbecks Arch Surg. 2009; 394: 105-13.". Langenbecks Arch Surg 2010;395:291-2.