Medicine®

CLINICAL CASE REPORT

OPEN

Case Report Series and Review of Rare Intradural Extramedullary Neoplasms–Bronchiogenic Cysts

Junchen Chen, Runlong Lai, Zhimin Li, Jun Gao, MD, PhD, Yongning Li, MD, Tianyu Wang, and Yong Li, MD

Abstract: The congenital malformation known as an intraspinal bronchiogenic cyst is a rare form of endodermal (neurenteric, enterogenous) cyst lined with respiratory tract epithelium. We describe 3 new cases of intradural extramedullary bronchiogenic cyst in the Department of Neurosurgery between the years 2006 and 2014. Three patients were performed resection of intradural extramedullary bronchiogenic cysts and finally symptoms were relieved. Taken together with 10 previous reports identified from a PubMed search, an analysis of 13 cases of intradural bronchiogenic cysts was conducted. The aim of this literature review was to provide information on histopathology, mechanisms of pathogenesis, clinical manifestations, radiographic features, and surgical strategies.

Symptoms in spinal bronchiogenic cyst patients primarily depend on the local mass effect of the cyst on the spinal cord. magnetic resonance imaging, together with myelograms and computed tomography scans, is necessary to preoperative evaluation of spinal bronchiogenic cysts. The aim of surgery is total resection, although tight adhesion, ventral and intramedullary locations, and vertebral anomalies make it more challenging.

(*Medicine* 94(49):e2039)

Abbreviations: CT = computed tomography, EMA = epithelial membrane antigen, FLAIR = fluid-attenuated inversion recovery, GFAP = glial fibrillary acidic protein, MRI = magnetic resonance imaging, T1WI = T1-weighted images, T2WI = T2-weighted images.

Editor: Liu Song.
Received: July 27, 2015; revised: September 25, 2015; accepted: October 20, 2015.
From the Department of Neurosurgery, First Affiliated Hospital of Shantou University Medical College, Shantou, Guangdong (JC, RL, YL); and Department of Neurosurgery, Peking Union Medical College Hospital, Chinese Academy of Medicine Sciences & Peaking Union Medical College, Beijing, China (ZL, JG, YL, TW).
Correspondence: Jun Gao, Department of Neurosurgery, Peking Union Medical College Hospital, Chinese Academy of Medicine Sciences & Peaking Union Medical College, No. 1 Shuaifuyuan Wangfujing Dongcheng District, Beijing 100730, China (e-mail: gaojunpumc@hotmail.com).
Ethical and conflict statement: Ethics committee approval is not included as it is commonly accepted that case reports do not require such approval. Because our work did not use patients' data that would allow identifying them, informed consent is not necessary.
Competing interests: We have no disclosures and did not receive any financial support.

ISSN: 0025-7974
DOI: 10.1097/MD.0000000000002039

INTRODUCTION

Bronchiogenic cyst is a congenital malformation representing one of the 3 types of endodermal cyst (neurenteric, enterogenous) covered with respiratory tract epithelium. Compared with sites such as the sternum, skin, stomach, and pericardium, bronchiogenic cysts in the spinal canal are rare.[1]

This report describes 3 new cases of intradural extramedullary bronchiogenic cyst, and reviews 10 previously documented cases to gain a better understanding of bronchiogenic cysts, including the histopathologic presentation, mechanisms of pathogenesis, clinical manifestations, radiographic features, and surgical strategies.

CASE PRESENTATION

Case 1

A 24-year-old male was admitted to hospital with progressive back pain for 1 month that sometimes radiated to both lower extremities. His family reported that he had a history of lumbosacral meningocele, which was surgically removed at 1 year of age. Neurologic examination revealed a thumping local pain in the lower lumbovertebral region and a positive Lasegue test on both sides at 70°. Magnetic resonance imaging (MRI) T1-weighted images (T1WI) demonstrated an L4 to L5 lesion displaying intermediate signal intensity without enhancement after gadolinium administration (Fig. 1A). The lesion was hyperintense on T2-weighted images (T2WI) (Fig. 1B). After performing a standard laminectomy of the L3 to L5 vertebrae, opening of the dura mater exposed a circumscribed, semitransparent pale cyst that was located dorsally to the filum terminale. It was difficult to completely excise the cystic mass because it was tightly attached to the filum terminale. Puncture of the cyst yielded a gelatinous, creamy-white liquid. Histopathologic examination of the surgical specimen was consistent with the features of a bronchiogenic cyst. The membrane was covered with respiratory, pseudostratified, ciliated columnar epithelium (Fig. 2A). After surgery, back and leg pain were both ameliorated. No relapsing intradural cystic mass was noted at follow-up MRI examinations.

Case 2

A 29-year-old male presented with a skin bulge in his lumbar area since13 years of age. He reported back pain for 1 month and numbness in the lower extremities for 1 week. Both medical history and neurologic examinations were unremarkable. Radiographs illustrated scoliosis in the lumbosacral region (Fig. 1C). Spinal MRI demonstrated an extramedullary lesion, which extended anteriorly from the T9 to T10 vertebrae, compressing the spinal cord. The cystic mass was hypointense on T1WIs and hyperintense in T2WIs. After gadolinium injection, there was no enhancement of the cystic extramedullary lesion (Fig. 1D). After performing a standard laminectomy at T8 to T10, the dura mater was opened, revealing a well defined, dark red,

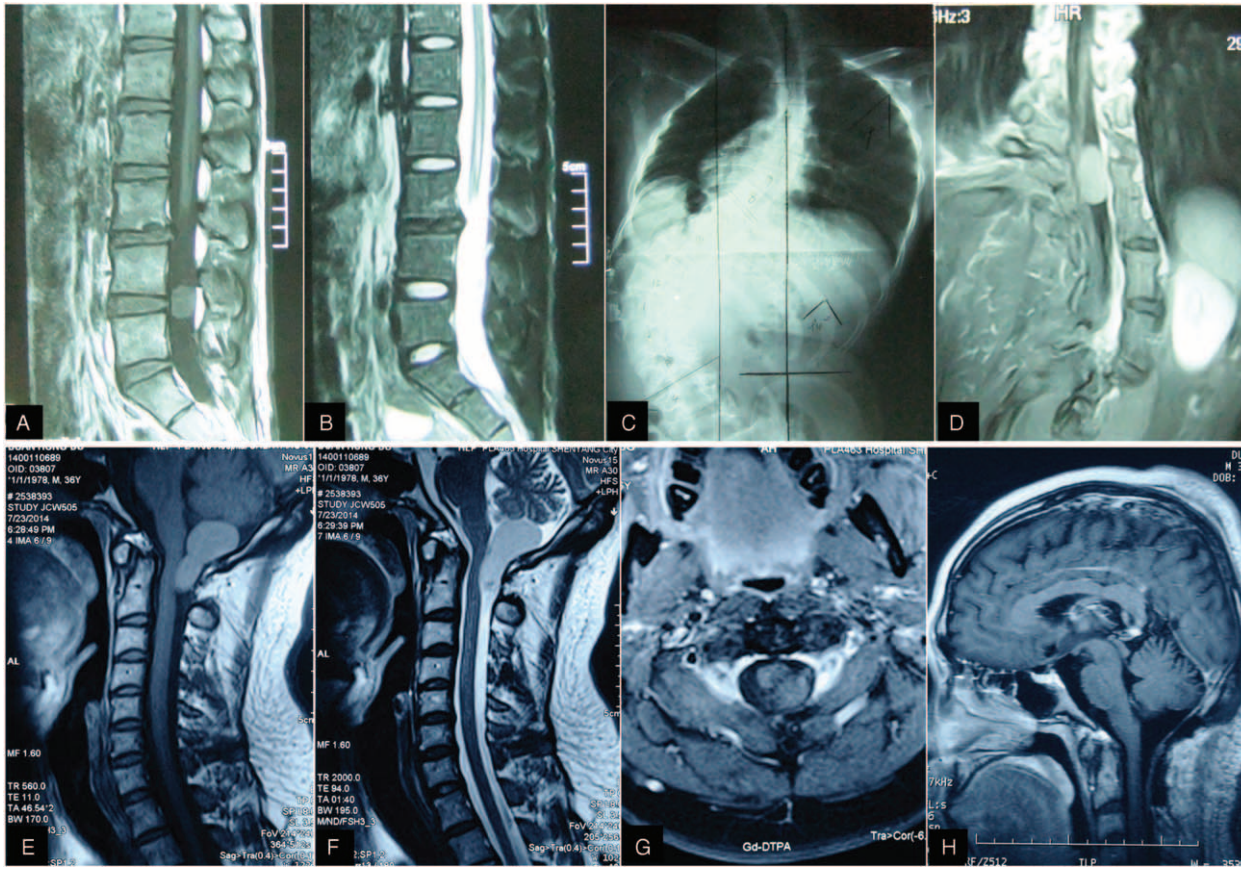

FIGURE 1. Radiographic images of the presenting cases. Case 1: (A) sagittal MRI demonstrates isointense signal on T1WI and (B) hyperintense signal on T2WI. Case 2: (C) scoliosis is seen in the X-ray examination. (D) An intradural extramedullary lesion at T9 to T10 is noted in the contrasted T1WI. Case 3: sagittal MRI illustrates (E) isointense lesion on T1WI and (F) slightly hyperintense signal on T2WI at craniocervical junction. (G) A corresponding axis MRI shows no enhancement after intravenous contrast material on T1WI. (H) No relapsing cystic mass is noted in the follow-up MRI examination. MRI = magnetic resonance imaging, T1WI = T1-weighted images, T2WI = T2-weighted images.

semitransparent cystic mass. The mass was tightly attached to the ventral aspect of the spinal cord such that it could not be completely resected. Histopathology analysis led to identification of the mass as a bronchiogenic cyst (Fig. 2B). The patient's symptoms were relieved after surgery.

Case 3

A 34-year-old male was admitted with neck pain and left leg numbness for the last 6 months. He had a 15-year history of chronic hepatitis B virus. Neurologic examinations revealed reduced pain and temperature sensations in the left leg. Cranial and spinal MRI findings revealed an extramedullary mass (9 mm × 18 mm × 16 mm) at the craniocervical junction. The lesion had a low-signal intensity on T1WIs and high-signal intensity on T2WIs, and was not enhanced after gadolinium injection (Fig. 1E–G). The patient underwent surgery using a suboccipital midline approach. A light-yellowish cystic mass was found in the cistern magna, extending from the lower part of the fourth ventricle to C2. The mass lesion was completely removed under the microscope (Fig. 2C). Light-yellow, viscous fluid was observed on puncture of the cystic mass. Histopathologic examination confirmed the diagnosis of bronchiogenic cyst (Fig. 2D). The patient had a favorable outcome, reporting that symptoms were diminished, and no relapse of the cystic mass on follow-up MRI examinations (Fig. 1H).

Literature Review

The literature search was performed with the PubMed search engine of the National Library of Medicine of the National Institutes of Health (http://www.ncbi.nlm.nih.gov/pubmed), using the following keywords: ''bronchiogenic cyst''; ''intradural extramedullary bronchiogenic cyst''; ''intradural bronchiogenic cyst''; ''spinal bronchiogenic cyst''; ''spinal bronchogenic cyst''; ''neurenetric cyst''; ''endodermal cyst''; ''enterdermal cyst''; ''respiratory''; ''spinal cord tumor''. The search was restricted to English-language publications without date limitations. Any case reports involving histopathologically confirmed intradural extramedullary bronchiogenic cysts were included. Intracranial bronchiogenic cysts were excluded.

A total of 10 patients were identified from the literature, and pooled with the 3 new cases described above. Clinical and radiologic findings for all 13 patients are shown in Table 1.

DISCUSSION

Histologically, congenital intraspinal cysts are classified into 3 types: epithelial, mesenchymal, and mixed (Table 2). The

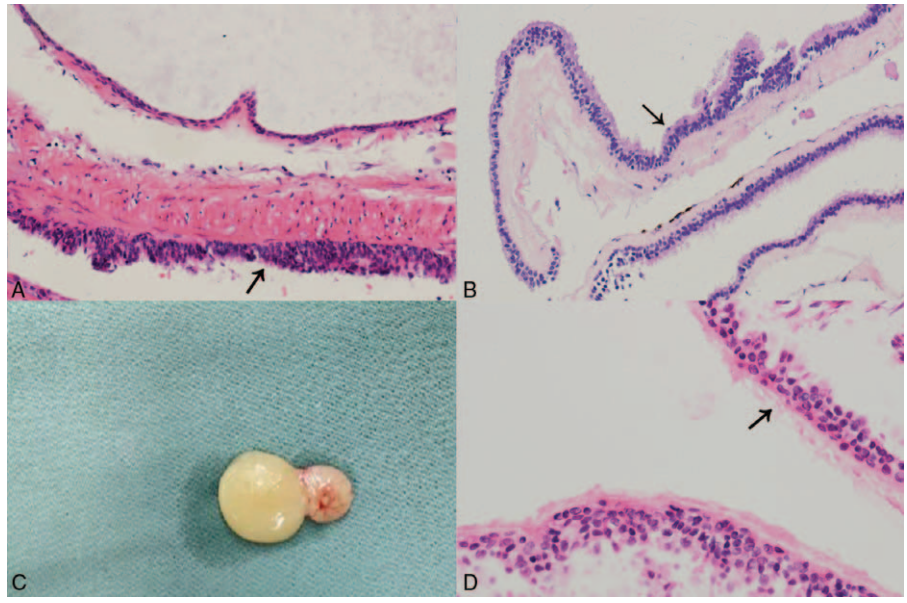

FIGURE 2. Histopathological appearances of the presenting cases. Case 1 (A), case 2 (B), and case 3 (D) demonstrating ciliated pseudostratified columnar epithelium (hematoxylin and eosin, ×200). Case 3 (C) presented the light-yellow gourd-shaped gross tumor after surgery.

epithelial group is further divided into either endodermal or ependymal cysts.[7] Previous studies show that definitions of intraspinal epithelial cysts are inconsistent. The variety of terms used to describe epithelial cysts, including enterogenous, endodermal, foregut, and neurenteric cysts, has led to confusion.[7,9] Brun and Saldeen[12] emphasized that the typical endodermal (neurenteric, enterogenous) cyst exhibits the following characteristics: gastrointestinal and/or respiratory epithelium without nonintestinal tissue components, a vertebral anomaly, and are most prevalent in the cervical and thoracic regions. The term ''bronchiogeni cyst'' refers to an endodermal cyst that is mainly lined with respiratory tract epithelium.[7]

Wilkins and Odom[13] categorized endodermal cysts into 3 types, according to histopathology. Type A cysts are the least complex, displaying a layer of cuboidal or columnar epithelium, with or without cilia, on a basement membrane composed of type IV collagen. Type B cysts have the characteristics of type A cysts, but are also characterized by a range of associated tissues, including smooth muscle, striated muscle, fat, cartilage, bone, elastic fibers, lymphoid tissue, and glandular components. Type C cysts display all the features of type A as well as glial or ependymal cells.

Other than histopathologic observations under the light microscope, immunohistochemistry may provide clues for the diagnosis of endodermal cysts.[14,15] Positive stain with antiepithelial membrane antigen (EMA) antibody and anticarcinoembryonic antigen antibody is suggestive of epithelial tissue, whereas endodermal cysts stain negative for glial fibrillary acidic protein (GFAP).

Although the pathogenesis of bronchiogenic cysts is currently unclear, several theories have been proposed. The most reasonable hypothesis is related to the concept of split notochord syndrome, which is likely to explain the pathogenesis of bronchiogenic cysts dorsal to the spinal cord. Bentley and Smith[16] concluded that the ventrally located yolk sac or gut anlage endoderm may herniate and rupture because of a partial duplication and separation of the notochord, resulting in a fistula between the yolk sac and the amniotic cavity. This fistula connects the future spinal cord and spine, and it closes when subsequent differential growth of the embryo is complete. Therefore, a cystic mass develops as a remnant of the foregut, which is capable of differentiating into tissues of the gut or its embryological derivatives.

In contrast, Fallon et al[17] and MeLetchie et al[18] postulated that ectodermal–endodermal adhesion in the early embryo leads to the occurrence of cysts. This theory may explain why these cysts are prevalent in the cervical and thoracic regions: the cephalic end of the notochord develops first, and organ development is easily disturbed during the initial stages.[2]

A third hypothesis was claimed by Rhaney and Barclay[19] who proposed that the cysts are of ectodermal origin, which can differentiate into both endoderm and paraxial mesoderm. However, this concept does not explain the pathogenesis of ventrally placed bronchiogenic cysts.

This literature review indicates that bronchiogenic cysts are predominately diagnosed in the first and second decades of life (61.5%), with a higher frequency in males (58.3%). The most common symptoms are associated with the local mass effect, and depend on the location of bronchiogenic cyst in the spinal canal. Patients commonly had pain in the neck or back, combined with radiating pain and motor and sensory disturbances in the extremities. The severity of symptoms may fluctuate because of the cyst columetric flux associated with periodic leakage of fluid content secondary to osmotic and hemodynamic factors.[14,20] According to MRI features and surgical findings, most bronchiogenic cysts were intradural extramedullary, with only 2 reported cases being intramedullary.[21,22] Ten of the bronchiogenic cysts were located dorsal to the spinal cord, whereas 3 were ventral to the spinal cord. The most frequent longitudinal location of bronchiogenic cysts was the cervical and upper thoracic levels (61.5%), consistent with previous findings.[12]

Magnetic resonance imaging is currently regarded as the best tool for diagnosis of spinal cord tumors because of

TABLE 1. Summary of Intradural Extramedullary Bronchiogenic Cyst Case Reports

Authors (y)	Age (y)/Sex	Location (Axial/Longitudinal)	MRI Features T1WI / T2WI/Enhancement		Anomalies	Outcome
Yamashita et al (1973)[2]	14/F	Dorsal/C6–C7	NR	NR	Spina bifida occulta	Relieved
Ho and Tiel (1989)[3]	21/F	Dorsal/C5–T3	NR	NR	No	NR
Wilkinson et al (1992)[4]	55/F	Dorsal/C3–C4	NR	NR	No	Relieved
Baba et al (1995)[5]	16/M	Dorsal/C1	Isointense	Hyperintense	No	Relieved
Rao et al (1999)[6]	18/M	Ventral/C2–C3	Hypointense	Hyperintense	No	Relieved
Baumann et al (2005)[7]	41/NR	Dorsal/T12–L1	NR	NR	Spina bifida occulta	Refractory
Chongyi et al (2008)[8]	28/M	Dorsal/L1	NR	Hyperintense	No	Relieved
Ko et al (2008)[9]	0/F	Dorsal/S2	Hypointense	Hyperintense	Spina bifida occulta	Relieved
Arnold et al (2009)[10]	20/M	Dorsal/T4	NR	Hyperintense	No	Relieved
Solaroglu et al (2013)[11]	50/F	Ventral/craniocervical junction	Isointense	Hyperintense	No	Relieved
Present case (2015)	24/M	Dorsal/L4–L5	Isointense	Hyperintense	No	Relieved
	34/M	Dorsal/Craniocervical junction	Hypointense	Hyperintense	No	Relieved
	29/M	Ventral/T9–T10	Isointense	Hyperintense	Scoliosis	Relieved

C = cervical, F = female, L = lumbar, M = male, NR = not reported, S = sacral, T = thoracic.

TABLE 2. Histology Classification and Diagnosis of Congenital Intraspinal Cysts

Classification	Histological Presentation
Epithelial	
Endodermal	
Type A	A layer of cuboidal or columnar epithelium, with or without cilia on a basement membrane composed of type IV collagen
Type B	Type A characteristics + a range of associated tissues, including smooth muscle, striated muscle, fat, cartilage, bone, elastic fibers, lymphoid tissue, and glandular components
Type C	Type A characteristics + glial or ependymal cells
Ependymal	
Mesenchymal	
Mixed	

improved resolution, fewer artifacts, and multiplanar images. From the MRI features provided in the previous studies, we conclude that most bronchiogenic cysts show low or intermediate signal intensity on T1WI and T2WI, without enhancement after intravenous contrast injection. In addition, fluid-attenuated inversion recovery (FLAIR) imaging is increasingly used to assist diagnosis. All cases of neurenteric cysts were hyperintense with cerebrospinal fluid on FLAIR sequences in Kimura et al's[23] study. Although MRI is superior for showing the relationship between the cystic mass and surrounding neural structures, myelograms and computed tomography (CT) are still considered as essential methods for excluding other congenital bony anomalies such as spina bifida occulta and scoliosis.[14] In this review, there were 3 patients with spina bifida occulta and 1 patient with scoliosis. Other bony abnormalities of the spine such as spinal dysraphism and Kippel–Fiel syndrome were described in previous neurenteric cyst case reports.[14]

Total surgical resection is the goal of treatment for bronchiogenic cysts. Partial resection is considered to increase the risk of recurrence because of the opportunity for remnant tissues to differentiate.[15] Garg et al[20] reported no recurrence in patients with gross total resection compared with 63% recurrence among patients with partial resection. In addition, cyst fenestration and biopsy are not recommended because of the possibility of widespread spinal dissemination.[15] It is easier to achieve total resection with intradural extramedullary cysts than intramedullary bronchiogenic cysts, which is attributed to clear inspection of the dissection plane between the cyst and spinal cord.[14] Other features that make it difficult to attain total resection include tight adhesion, ventral location, and vertebral anomalies. The majority of patients had a favorable result after surgery, without relapse of the cystic mass in follow-up MRI examinations, except for 1 patient who did not have symptomatic remission. Of note, neurenteric cysts have also been associated with other rare complications such as *Staphylococcus aureus* infection, spontaneous hemorrhage, and malignant transformation.[24,25]

CONCLUSIONS

Spinal bronchiogenic cysts are rare congenital malformations, which are characterized in histopathology as endodermal (neurenteric, enterogenous) cysts covered with

respiratory tract epithelium. Although their pathogenesis is still unclear; 3 main hypotheses have been proposed. Symptoms primarily depend on the local mass effect of the cyst on the spinal cord. MRI features of bronchiogenic cysts include isointense or hypointense signals on T1WI, no enhancement on contrasted T1WI, and hyperintense signals on T2WI and FLAIR. Myelograms and CT scans are necessary to exclude the presence of congenital bony anomalies. The aim of surgery is total resection. However, tight adhesion, ventral and intramedullary locations, and vertebral anomalies make it more challenging to achieve complete resection. Although almost all patients in this review had a good result; however, partial resection, cystic fenestration, and biopsy should be avoided because of higher recurrence rates.

ACKNOWLEDGMENTS

We thank the Department of Pathology, Peaking Union Medical College Hospital for supervising all pathological analyses.

REFERENCES

1. Ko CL, Lin HJ, Foo NP, Chen KT. Bronchogenic cyst. *J Emerg Med.* 2010;39:650–651.
2. Yamashita J, Maloney AF, Harris P. Intradural spinal bronchiogenic cyst. Case report. *J Neurosurg.* 1973;39:240–245.
3. Ho KL, Tiel R. Intraspinal bronchogenic cyst: ultrastructural study of the lining epithelium. *Acta Neuropathol.* 1989;78:513–520.
4. Wilkinson N, Reid H, Hughes D. Intradural bronchogenic cysts. *J Clin Pathol.* 1992;45:1032–1033.
5. Baba H, Okumura Y, Ando M, Imura S, Morioka K, Noriki S. A high cervical intradural extramedullary bronchogenic cyst. Case report. *Paraplegia.* 1995;33:228–232.
6. Rao GP, Bhaskar G, Reddy PK. Cervical intradural extramedullary bronchiogenic cyst. *Neurol India.* 1999;47:79–81.
7. Baumann CR, Konu D, Glatzel M, Siegel AM. Thoracolumbar intradural extramedullary bronchiogenic cyst. *Acta Neurochir (Wien).* 2005;147:317–319discussion 319.
8. Chongyi S, Meng Y, Dejun Y, Yingjie L, Qingpeng L. Lumbar intradural extramedullary bronchiogenic cyst. *Eur Surg Res.* 2008;40:26–28.
9. Ko KS, Jeun SS, Lee YS, Park CK. Sacral intraspinal bronchogenic cyst: a case report. *J Korean Med Sci.* 2008;23:895–897.
10. Arnold PM, Neff LL, Anderson KK, Reeves AR, Newell KL. Thoracic myelopathy secondary to intradural extramedullary bronchogenic cyst. *J Spinal Cord Med.* 2009;32:595–597.
11. Solaroglu I, Algin O, Caylak B, Keles GE. Bronchogenic cyst of the craniocervical junction: a case report. *Turk Neurosurg.* 2014;24:284–287.
12. Brun A, Saldeen T. Intraspinal enterogenous cyst. *Acta Pathol Microbiol Scand.* 1968;73:191–194.
13. Wilkins RH, Odom GL. Tumors of the spine and spinal cord, part 2. In: Vinken PJ, Bruyn GW, editors. Handbook of clinical neurology. Amsterdam; 1976. p. 55–102.
14. Savage JJ, Casey JN, McNeill IT, Sherman JH. Neurenteric cysts of the spine. *J Craniovertebr Junction Spine.* 2010;1:58–63.
15. Gauden AJ, Khurana VG, Tsui AE, Kaye AH. Intracranial neuroenteric cysts: a concise review including an illustrative patient. *J Clin Neurosci.* 2012;19:352–359.
16. Bentley JF, Smith JR. Developmental posterior enteric remnants and spinal malformations: the split notochord syndrome. *Arch Dis Child.* 1960;35:76–86.
17. Fallon M, Gordon AR, Lendrum AC. Mediastinal cysts of fore-gut origin associated with vertebral abnormalities. *Br J Surg.* 1954;41:520–533.
18. McLetchie NG, Purves JK, Saunders RL. The genesis of gastric and certain intestinal diverticula and enterogenous cysts. *Surg Gynecol Obstet.* 1954;99:135–141.
19. Rhaney K, Barclay GP. Enterogenous cysts and congenital diverticula of the alimentary canal with abnormalities of the vertebral column and spinal cord. *J Pathol Bacteriol.* 1959;77:457–471.
20. Garg N, Sampath S, Yasha TC, Chandramouli BA, Devi BI, Kovoor JM. Is total excision of spinal neurenteric cysts possible. *Br J Neurosurg.* 2008;22:241–251.
21. Yilmaz C, Gulsen S, Sonmez E, Ozger O, Unlukaplan M, Caner H. Intramedullary bronchogenic cyst of the conus medullaris. *J Neurosurg Spine.* 2009;11:477–479.
22. Wakao N, Imagama S, Ito Z, et al. A case of split notochord syndrome: an adult with a spinal endodermal cyst mimicking an intramedullary tumor. *Neuropathology.* 2011;31:626–631.
23. Kimura H, Nagatomi A, Ochi M, Kurisu K. Intracranial neurenteric cyst with recurrence and extensive craniospinal dissemination. *Acta Neurochir (Wien).* 2006;148:347–352discussion 352.
24. Perry A, Scheithauer BW, Zaias BW, Minassian HV. Aggressive enterogenous cyst with extensive craniospinal spread: case report. *Neurosurgery.* 1999;44:401–404[discussion 404–405].
25. Hicdonmez T, Steinbok P. Spontaneous hemorrhage into spinal neurenteric cyst. *Childs Nerv Syst.* 2004;20:438–442.