Article published online: 2022-03-14

Enterogenous Cyst and Glioblastoma: A Brief Histopathological Review of Two Uncommon Cystic Lesions of the Central Nervous System

Cisto entérico e glioblastoma: Uma breve revisão histopatológica de duas lesões císticas incomuns do sistema nervoso central

Eduardo Cambruzzi[1–5] Nelson Pires Ferreira[2] Marcelo Paglioli Ferreira[2] Guilherme Gago[2] João Pedro Pattussi Bertinatti[2]

[1] Universidade Federal do Rio Grande do Sul, Porto Alegre, RS, Brazil.
[2] Complexo Hospitalar Santa Casa, Porto Alegre, RS, Brazil.
[3] Hospital Nossa Senhora da Conceição, Porto Alegre, RS, Brazil.
[4] Instituto de Cardiologia, Fundação Universitária de Cardiologia, Porto Alegre, RS, Brazil.
[5] Universidade do Vale do Rio do Sinos, São Leopoldo, Rio Grande do Sul, Brazil

Address for correspondence Eduardo Cambruzzi, PhD, Department of Pathology, Hospital Santa Rita, Complexo Hospitalar Santa Casa, Rua Sarmento Leite, 187, 2° andar, Porto Alegre, RS, Brazil (e-mail: dudacambruzzi@yahoo.com.br).

Arq Bras Neurocir 2022;41(2):e192–e197.

Abstract

Intracranial cystic lesions are common findings in cerebral imaging and might represent a broad spectrum of conditions. These entities can be divided into nonneoplastic lesions, comprising Rathke cleft cyst, arachnoid cyst, and colloid cyst, as well as neoplastic lesions, including benign and malignant components of neoplasms such as pilocytic astrocytoma, hemangioblastoma, and ganglioglioma. Surgical resection and histological evaluation are currently the most effective methods to classify cysts of the central nervous system. The authors report two uncommon cases presenting as cystic lesions of the encephalic parenchyma—a enterogenous cyst and a glioblastoma—and discuss typical histological findings and differential diagnosis.

Keywords
- brain cyst
- glioblastoma
- central nervous system
- pathology
- prognosis

Resumo

Lesões císticas intracranianas são achados comuns em imagens cerebrais e podem representar um amplo espectro de condições. Essas entidades podem ser divididas em lesões não neoplásicas, compreendendo cisto da bolsa de Rathke, cisto aracnoide e cisto colóide, e lesões neoplásicas, incluindo componentes benignos e malignos de neoplasias, como astrocitoma pilocítico, hemangioblastoma e ganglioglioma. A ressecção cirúrgica e a avaliação histológica são atualmente os métodos mais eficazes para classificar os cistos do sistema nervoso central. Os autores relatam dois casos incomuns que se apresentam como lesões císticas do parênquima encefálico, um cisto entérico e um glioblastoma, e discutem achados histológicos típicos e diagnósticos diferenciais.

Palavras-chave
- cisto cerebral
- glioblastoma
- sistema nervoso central
- patologia
- prognóstico

received
November 13, 2021
accepted
February 2, 2022
published online
March 14, 2022

DOI https://doi.org/10.1055/s-0042-1744112.
ISSN 0103-5355.

Thieme Revinter Publicações Ltda., Rua do Matoso 170, Rio de Janeiro, RJ, CEP 20270-135, Brazil

Introduction

Cystic lesions of the central nervous system (CNS) parenchyma comprise distinct pathological entities.[1–3] Benign cystic process arising in CNS include arachnoid cyst, epidermoid and dermoid cysts, colloid cyst, ependymal cyst, pineal cyst, Rathke cleft cyst, or even infectious diseases such as cysticercosis and abscesses.[1–4] Slow-growing CNS neoplasms such as ganglioglioma, hemangioblastoma, and pilocytic astrocytoma may exhibit cystic areas. Cysts differ from cystic neoplasms in that they lack a solid nodular area.[1,2,4] This typical finding is fundamental to distinguish glial cysts from cystic gliomas with mural nodules, and cystic craniopharyngiomas from epithelial cysts. In adults, glioblastomas and metastatic carcinomas can develop into cystic variations.[1,4,5] Mural nodule biopsy is recommended to obtain an accurate diagnosis. However, in some cases, the mural nodule may be difficult to detect.[2,4–6] In this case report, the authors describe two distinct cystic lesions, a developmental disorder and a high-grade glial neoplasm, to discuss characteristic histological findings and differential diagnosis.

Case 1

A 60-year-old female patient presented with an incidental finding of an expansive brain lesion during hospitalization for coronavirus disease 2019 (COVID-19). The patient reported frequent episodes of chronic headache, systemic arterial hypertension, dyslipidemia, patent foramen ovale, and myocardial revascularization. Neurological examination showed no abnormality. Magnetic resonance imaging (MRI) revealed a cystic lesion near the suprasellar cistern (►**Fig. 1**), extending toward the interpeduncular cistern and defining a bulging area of the inferior wall of the third ventricle, with obliteration of the infundibular recess. The signal intensity of the lesion was similar to that of the cerebral spinal fluid, and the lesion measured 4.6 × 3.6 × 3.5 cm (►**Fig. 2**).

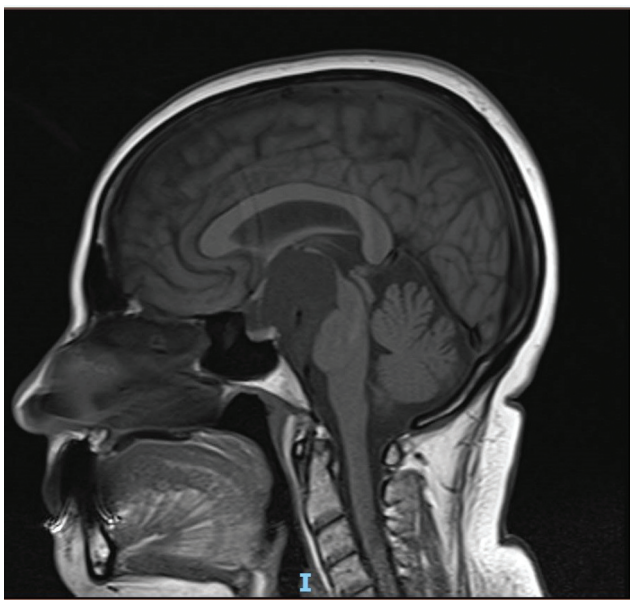

Fig. 1 Enterogenous cyst: MRI exhibiting a cystic lesion near the suprasellar cistern.

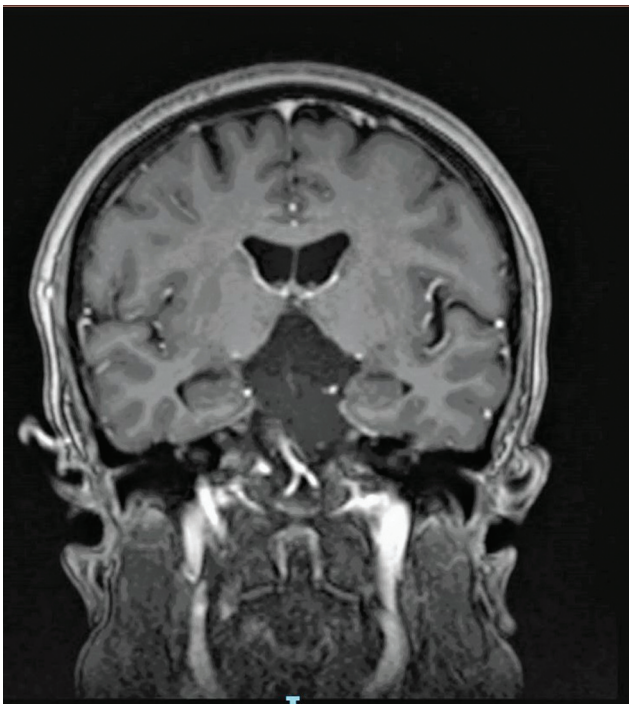

Fig. 2 Enterogenous cyst: MRI showing a cystic lesion measuring 4.6 × 3.6 × 3.5 cm and arising in inferior wall of the third ventricle.

The patient underwent left pterional craniotomy, dissection of the Sylvian fissure, and visualization and resection of the lesion close to the interpeduncular fossa. The specimen was sent for anatomopathological examination with a clinical–surgical hypothesis of a parasitic lesion. Microscopic examination of the process revealed a benign cystic lesion with walls consisting of connective tissue and internally covered by cuboidal and/or cylindrical epithelium, sometimes simple, sometimes pseudostratified, with ciliated or muciparous cells (►**Fig. 3**), compatible with an enterogenous cyst.

Case 2

An 18-year-old, previously healthy, male patient was referred to the hospital with complaints of severe headache and hypertensive peaks associated with temporary deviation of the rima oris for the past 7 days. He also reported episodes of fever, tremors, and sweating. On physical examination, the patient was somnolent and disoriented, with dysarthria, left hemiparesis, and a score of 13 on the Glasgow scale. Computed tomography and MRI revealed a solid cystic lesion in the topography of the third ventricle, measuring 5.4 × 5.0 × 4.7 cm (►**Fig. 4**) and causing hydrocephalus, compression of the interpeduncular region of the midbrain, a significant reduction in the amplitude of perimesencephalic cisterns, and cerebral edema, (►**Fig. 5**) suggestive of craniopharyngioma. The patient developed nausea, vomiting, intracranial hypertension, and Parinaud syndrome.

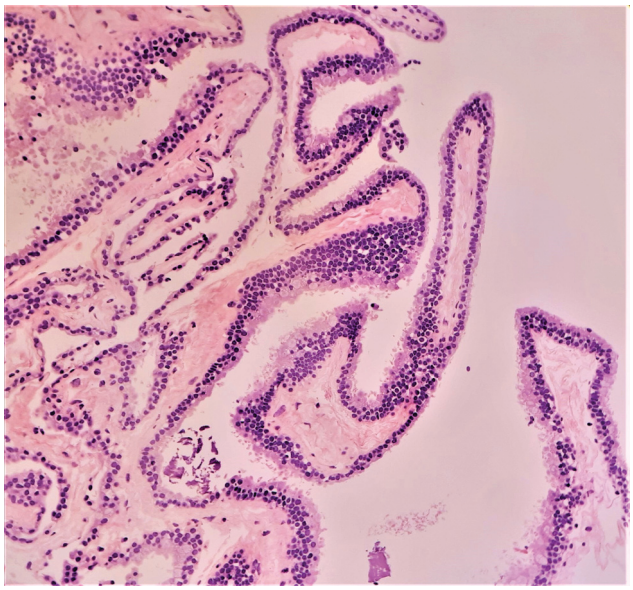

Fig. 3 Enterogenous cyst: benign cystic lesion covered by cuboidal and/or cylindrical epithelium, hematoxylin-eosin, 100x.

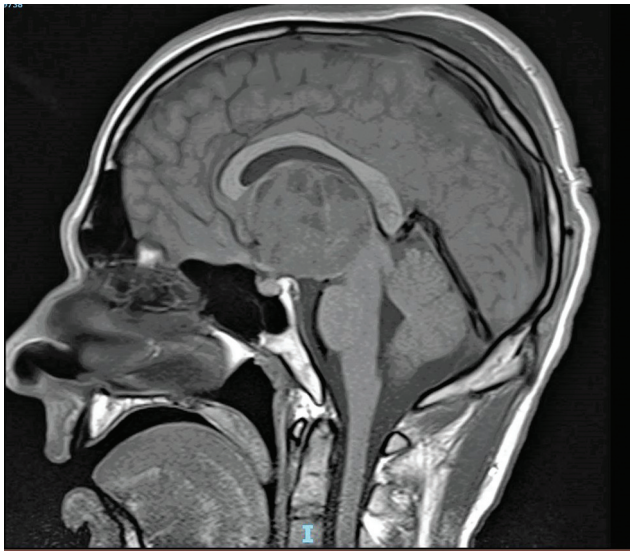

Fig. 4 Glioblastoma: MRI revealed a solid cystic lesion in the topography of the third ventricle.

External ventricular drainage was performed, leading to partial improvement of symptoms. The patient progressed to spasticity, anisocoria without light reflexes, tachycardia, tachypnea, and decorticate and decerebrate posturing, with no eye opening. Orotracheal intubation was then performed. The electroencephalogram showed slow and dysfunctional background activities, dominated by diffuse delta waves and a small amount of superimposed theta activity, compatible with diffuse dysfunction of brain activity without epileptiform paroxysms. The patient underwent resection of the lesion. Pathological examination revealed a poorly differentiated, pleomorphic, malignant neoplasm characterized by epithelioid/polygonal cells with high mitotic index and areas of necrosis (►**Fig. 6**).

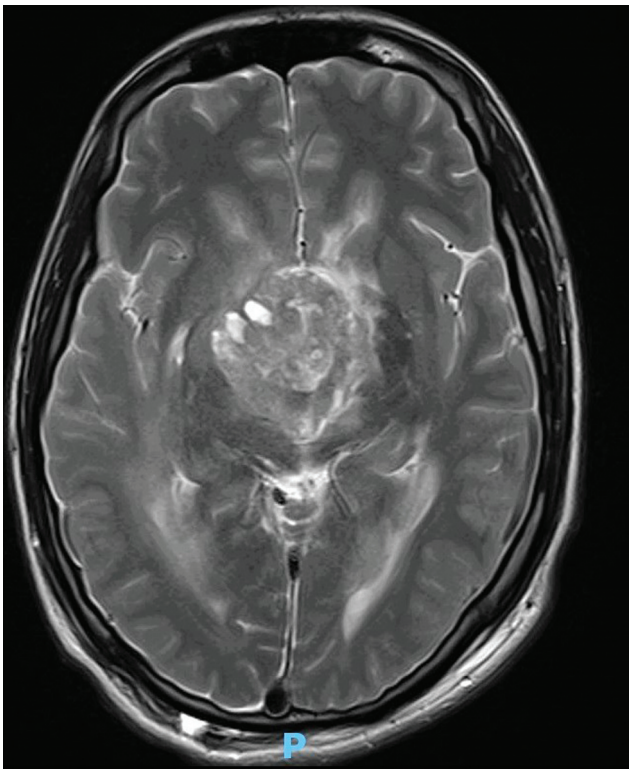

Fig. 5 Glioblastoma: MRI exhibiting a solid-cystic lesion, which determined hydrocephalus, compression of the interpeduncular region of the midbrain, a reduction of perimesencephalic cisterns, and edema.

The lesion exhibited strong and diffuse positive immunoexpression for GFAP, OLIG2, synaptophysin, CD99, INI-1, and ATRX, and was negative for IDH, p53, H3K27M, PHOX2B, SALL4, and HCG. The K_i-67 expression was observed in 95% of neoplastic cells (►**Fig. 7**). These histopathological findings were compatible with glioblastoma associated with an area of primitive neuroectodermal characteristics and some giant tumor cells, grade 4 according to the World Health Organization (WHO) 2021 system.

The patient evolved with diabetes insipidus, central hypothyroidism, secondary adrenal insufficiency, fever, leukocytosis with deviation, thrombosis in the left upper limb, progressive worsening of the neurological condition, and nonreactive mydriasis associated with septic shock. Death occurred 9 weeks after the surgical procedure.

Discussion

Intracranial cystic lesions are a heterogeneous group of processes, including parasitic infections, abscesses, developmental cysts, and primary and metastatic neoplasms.[1,2,4] In the case of primary and metastatic neoplasms, analysis of medical history often leads to the correct diagnosis.[1,2,4] Recently, imaging, especially new MRI techniques, has proven to be particularly useful for the diagnosis of these challenging lesions. However, it is only after histological analysis that a definite diagnosis can be made.[2,4–6]

Infectious diseases, such as neurocysticercosis, echinococcosis, cryptococcosis, tuberculosis, amebiasis, and

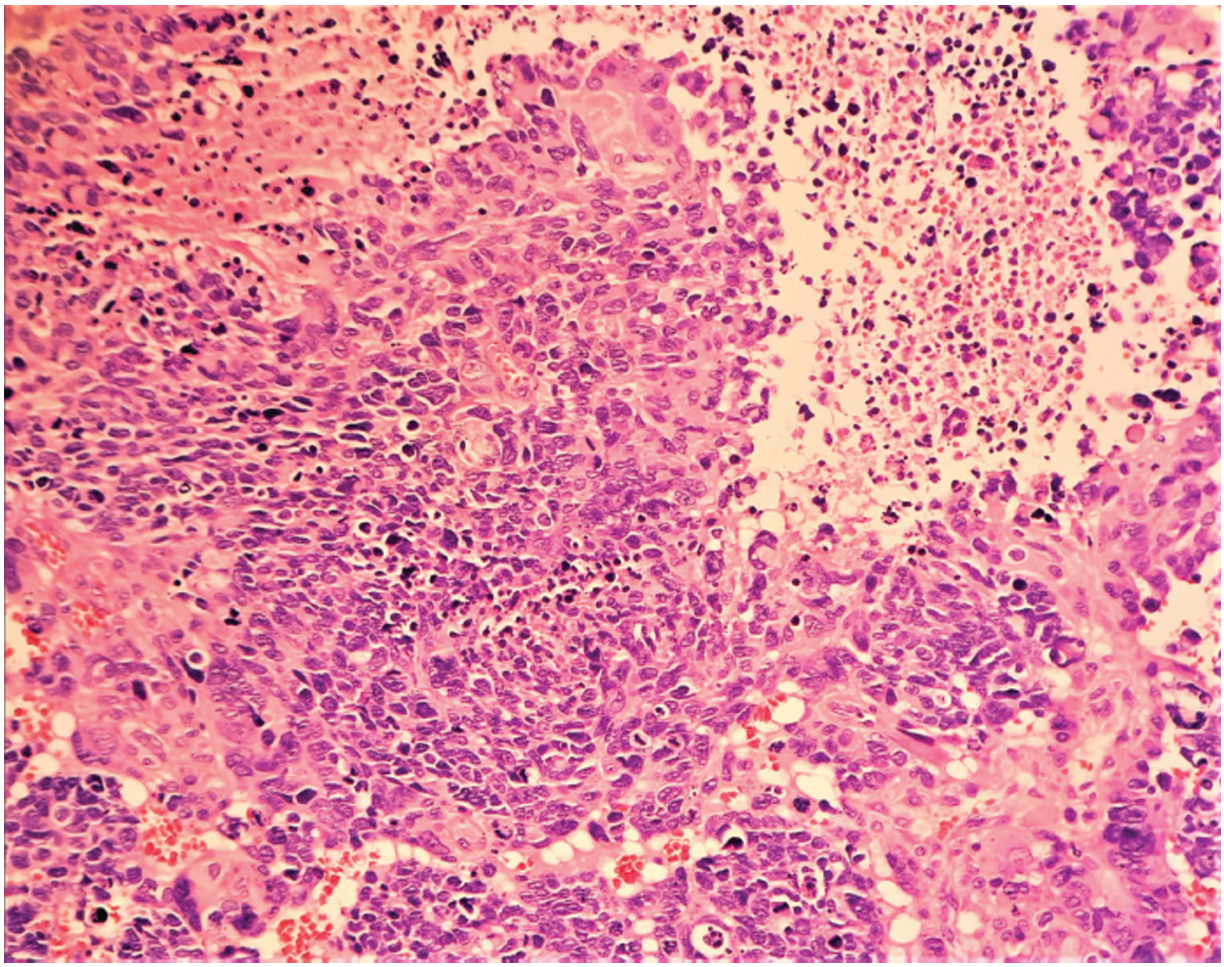

Fig. 6 Glioblastoma: A high-grade glioma with high mitotic index and necrosis, hematoxylin-eosin, 200x.

toxoplasmosis, are often suspected in patients with a cyst, as revealed by imaging, and presenting with severe headache, convulsion, fever, or delirium. By contrast, incidentally found intracranial cysts are commonly congenital.[2,4,5,7] Arachnoid, pineal, epidermoid, dermoid, ependymal, Rathke cleft, and enterogenous cysts are some of the nonneoplastic diagnostic possibilities.[2,5,7–9] Benign neoplastic intracranial diseases include craniopharyngiomas, usually suspected when located at the suprasellar region, having excellent survival rates. Intratumoral necrosis or hemorrhage is responsible for cystic presentation of both intracranial metastases and higher-grade primary tumors. The former usually presents as a multifocal lesion.[1,5,7–10]

In our first report, we described a rare case of an intracranial enterogenous cyst, also called endodermal cyst. This entity is a benign developmental lesion of endodermal origin.[2,3,11–13] Its pathogenesis is not fully understood, but probably arises after failure of obliteration of the neurenteric canal, with displacement of endodermal cells. It is more commonly found in the spine, rarely as an encephalic lesion.[2,11–13] Histologically, the cyst is lined by gastrointestinal or respiratory-type epithelium, with or without cilia, cuboidal to columnar, and simple to pseudostratified. It is sometimes impossible to histologically distinguish a Rathke cleft cyst from an enterogenous cyst; the former is often diagnosed when the lesion is intra- or suprasellar.[1,5,7,8,13,14] Given the nonneoplastic nature of enterogenous cysts, symptoms depend on lesion size and location, ranging from headaches (in almost 50% of patients) to seizures and deficits. Treatment in most cases is by surgical resection. Follow-up is recommended, as recurrence is common.[1,5,7,8,14,15]

In our second report, we described the case of an H3-/IDH-wildtype glioblastoma, with giant cells and primitive neuroectodermal component, presenting as an acute, aggressive, solid cystic lesion of the third ventricle. Glioblastoma is a high-grade glioma featuring nuclear atypia, pleomorphism, mitotic activity, diffuse growth pattern, microvascular proliferation, and necrosis.[1,4,7,11,15,16] It is the most frequent malignant brain tumor in adults, very rarely occurring in the pediatric population. In the latter case, the malignancy is defined as pediatric-type high-grade diffuse glioma, according to the 2021 WHO CNS classification.[10] Glioblastomas develop rapidly, primarily manifesting as focal neurological deficits, as in our case. Imaging reveals irregularly shaped and ring-shaped zones of contrast enhancement around a dark central area of necrosis, sometimes interpreted as a cystic area in the lesion.[2,3,10,14,16,17] Surgical excision is the primary

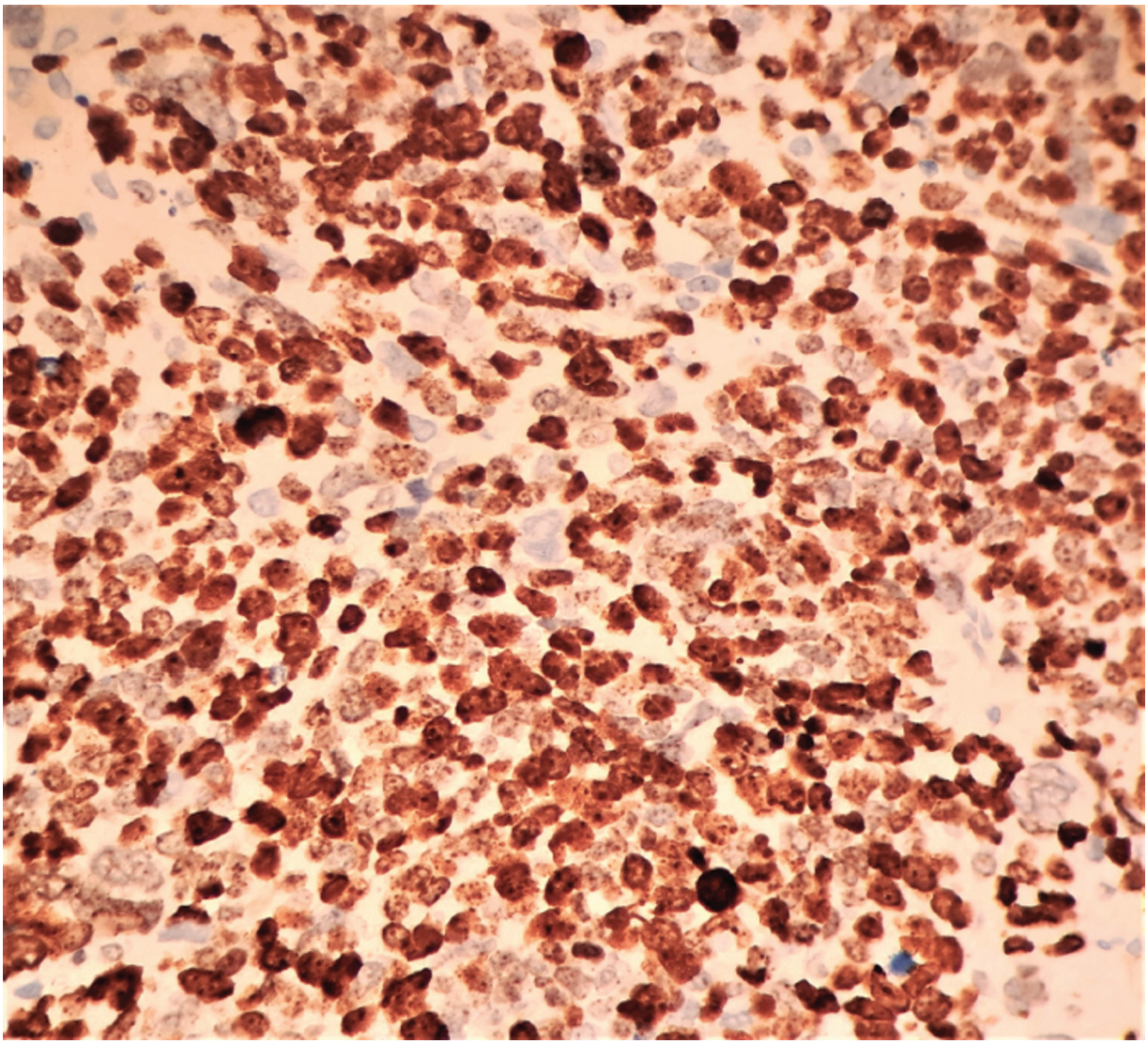

Fig. 7 Glioblastoma: High proliferative index estimated by K_i-67 imunoexpression, Ventana Systems, 400x.

treatment, although the disease is almost invariably fatal. An abrupt change in morphology may reflect new clone proliferation through new genetic alterations.[1,2,5,9,10] The primitive neuronal component represents a variation in glioblastoma, with one or more solid-looking nodules showing primitive neuronal morphology sharply demarcated from adjacent glioma, markedly increased cellularity, higher N/C ratio, mitotic activity, karyorrhexis, and anaplastic cytology similar to that of other CNS embryonal neoplasms.[2,3,5,7,8,11,13,17] It usually shows synaptophysin positivity, loss of GFAP expression, and a high K_i-67 index. This subtype has a high frequency of MYC gene amplification and p53 immunoreactivity. Although the survival time is similar to that of other glioblastomas,[9] our case presented as a very aggressive acute disease, with 2 months from first symptoms to death.[1,5,9,10,18] We add this unfortunate case to the very few literature reports of this aggressive high-grade glioma variant in the pediatric population.

Conflict of Interests
The authors have no conflict of interests to declare.

References

1 Oprişan A, Popescu BO. Intracranial cysts: an imagery diagnostic challenge. ScientificWorldJournal 2013;2013:172154
2 Osborn AG, Preece MT. Intracranial cysts: radiologic-pathologic correlation and imaging approach. Radiology 2006;239(03): 650–664
3 Taillibert S, Le Rhun E, Chamberlain MC. Intracranial cystic lesions: a review. Curr Neurol Neurosci Rep 2014;14(09): 481
4 Rapalino O, Mullins ME. Intracranial Infectious and Inflammatory Diseases Presenting as Neurosurgical Pathologies. Neurosurgery 2017;81(01):10–28
5 Anderson T, Kaufman T, Murtagh R. Intracranial neurenteric cyst: A case report and differential diagnosis of intracranial cystic lesions. Radiol Case Rep 2020;15(12):2649–2654
6 Larkin SJ, Ansorge O. Pathology and pathogenesis of craniopharyngiomas. Pituitary 2013;16(01):9–17

7 Chen CT, Lai HY, Jung SM, Lee CY, Wu CT, Lee ST. Neurenteric Cyst or Neuroendodermal Cyst? Immunohistochemical Study and Pathogenesis. World Neurosurg 2016;96:85–90
8 Preece MT, Osborn AG, Chin SS, Smirniotopoulos JG. Intracranial neurenteric cysts: imaging and pathology spectrum. AJNR Am J Neuroradiol 2006;27(06):1211–1216
9 Miller CM, Wang BH, Moon SJ, Chen E, Wang H. Neurenteric cyst of the area postrema. Case Rep Neurol Med 2014;2014:718415
10 Louis DN, Perry A, Wesseling P, et al. The 2021 WHO Classification of Tumors of the Central Nervous System: a summary. Neuro-oncol 2021;23(08):1231–1251
11 Georgiu C, MihuȚ E, Raus I, Mirescu ŞC, Szabo L, Şovrea AS. Pediatric glioblastoma with giant cells and "supratentorial" primitive neuroectodermal component - case report and review of the literature. Rom J Morphol Embryol 2015;56(03):1165–1171
12 McNutt SE, Mrowczynski OD, Lane J, et al. Congenital spinal cysts: an update and review of the literature. World Neurosurg 2021; 145:480–491.e9
13 Youssef A, D'Antonio F, Khalil A, et al. Outcome of fetuses with supratentorial extra-axial intracranial cysts: a systematic review. Fetal Diagn Ther 2016;40(01):1–12
14 Hirano A, Hirano M. Benign cysts in the central nervous system: neuropathological observations of the cyst walls. Neuropathology 2004;24(01):1–7
15 Brinkmeier ML, Bando H, Camarano AC, et al. Rathke's cleft-like cysts arise from Isl1 deletion in murine pituitary progenitors. J Clin Invest 2020;130(08):4501–4515
16 Savas Erdeve S, Ocal G, Berberoglu M, et al. The endocrine spectrum of intracranial cysts in childhood and review of the literature. J Pediatr Endocrinol Metab 2011;24(11-12):867–875
17 Utsuki S, Oka H, Suzuki S, et al. Pathological and clinical features of cystic and noncystic glioblastomas. Brain Tumor Pathol 2006;23 (01):29–34
18 Alongi P, Vetrano IG, Fiasconaro E, et al. Choline-PET/CT in the differential diagnosis betwen cystic glioblastoma and intraparenchymal hemorrhage. Curr Radiopharm 2019;12(01):88–92

