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

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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

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.

Keywords ► cisto cerebral ► glioblastoma ► sistema nervoso central ► patologia ► prognóstico

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Introduction

Cystic lesions of the central nervous system (CNS) parenchyma comprise distinct pathological entities.\textsuperscript{1–3} Benign cystic process arising in CNS include arachnoid cyst, epi- dermoid and dermoid cysts, colloid cyst, ependymal cyst, pineal cyst, Rathke cleft cyst, or even infectious diseases such as cysticercosis and abscesses.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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 (\textbullet\textsuperscript{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 (\textbullet\textsuperscript{Fig. 2}).

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 (\textbullet\textsuperscript{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 (\textbullet\textsuperscript{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, (\textbullet\textsuperscript{Fig. 5}) suggestive of craniopharyngioma. The patient developed nausea, vomiting, intracranial hypertension, and Parinaud syndrome.
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).

The lesion exhibited strong and diffuse positive immunoreexpression for GFAP, OLIG2, synaptophysin, CD99, INI-1, and ATRX, and was negative for IDH, p53, H3K27M, PHOX2B, SALL4, and HCG. The Ki-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. In the case of primary and metastatic neoplasms, analysis of medical history often leads to the correct diagnosis. 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.

Infectious diseases, such as neurocysticercosis, echinococcosis, cryptococcosis, tuberculosis, amebiasis, and
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.\textsuperscript{2,4,5,7} Arachnoid, pineal, epidermoid, dermoid, ependymal, Rathke cleft, and enterogenous cysts are some of the nonneoplastic diagnostic possibilities.\textsuperscript{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.\textsuperscript{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.\textsuperscript{2,3,11–13} Its pathogenesis is not fully understood, but probably arises after failure of obliteration of the neuroenteric canal, with displacement of endodermal cells. It is more commonly found in the spine, rarely as an encephalic lesion.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{2,3,10,14,16,17} Surgical excision is the primary

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{glioblastoma.png}
\caption{Glioblastoma: A high-grade glioma with high mitotic index and necrosis, hematoxylin-eosin, 200x.}
\end{figure}
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 Ki-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

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