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Radiation-induced CNS tumor in children: a diagnostic challenge

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Abstract: Neuroradiology plays an important role in the diagnosis of CNS tumors, both in defining treatment and in short and long-term follow-up. Diffusion and its correlation with ADC is a modality that has recently become relevant to establish the degree of malignancy of certain tumors, such as CNS gliomas. Gliomas are the most frequent CNS tumors in pediatrics, constituting 47% of these. We present a clinical case of a pediatric patient diagnosed with posterior fossa medulloblastoma and a radiation-induced tumor (high-grade glioma), diagnosed four years after radiotherapy, which presented difficulties in neuroradiological diagnosis due to its unusual characteristics. It continues to be a challenge for current neuroradiology to be able to establish the etiology of CNS lesions in cancer patients before surgical treatment.

Key words: central nervous system neoplasms; glioma; pediatrics; radiation-induced tumor

1 Introduction

Neuroradiology plays an important role in the diagnosis of central nervous system (CNS) tumors, both in determining treatment and in short-term and long-term follow-up. Magnetic resonance imaging (MRI) is a modality that allows for the detection of CNS tumors. Advanced imaging techniques, such as diffusion-weighted imaging (DWI), apparent diffusion coefficient (ADC), spectroscopy, and perfusion imaging, provide insights into tumor microstructure, pathophysiological changes, tissue function, and properties, offering an approach to molecular diagnosis [1-3]. In 2016, the World Health Organization (WHO) introduced molecular biology as a determinant for the classification of CNS tumors and as a tool for establishing prognosis and therapeutic response [4].

Gliomas are the most common CNS tumors in pediatrics, accounting for 47% of them. They can be classified based on the glial cell of origin and range from low-grade gliomas to high-grade gliomas [5,6].

Low-grade gliomas are a heterogeneous group of lesions characterized by being localized, minimally infiltrative, slow-growing tumors with an excellent prognosis and long-term survival with currently available treatments [2,6].

High-grade gliomas, on the other hand, are diffuse, highly infiltrative lesions that carry a poor prognosis, with a two-year survival rate of 10–30% [2,6].

The occurrence of a second tumor in pediatrics—defined as a new neoplasm histologically distinct from the first tumor, occurring after exposure to radiation therapy and not associated with phakomatosis—is a rare complication, but one that must be kept in mind in the pediatric population, given the increased survival rates achieved through advances in

cancer treatment and high exposure to ionizing radiation. This is a multifactorial event that depends on age, genetic predisposition, and the treatment received, among other variables. Cranial radiation therapy is a known significant risk factor for the development of a second neoplasm [7].

2 Clinical case

We present the case of a 9-year-old patient diagnosed with posterior fossa medulloblastoma with intracranial metastases at diagnosis (third ventricle), who was treated with subtotal surgical resection (2017), craniospinal radiotherapy (with a boost to the posterior fossa), and chemotherapy (completed in 2018) (Figure. 1).

Due to presenting with hydrocephalus, he required the placement of a ventriculoperitoneal shunt (VPS), which developed infectious complications, ultimately resulting in the placement of an externally adjustable VPS.

He continued with clinical and imaging follow-up according to protocol, during which no signs of radiation-induced lesions in the brain parenchyma were observed in subsequent annual follow-ups.

On the follow-up MRI, four years after the completion of treatment (2022), a focal lesion is observed in the right posterior temporal lobar white matter, the center of which shows signal isointense with cerebrospinal fluid (CSF) without restriction on DWI, with a wall that is subtly hypointense on T2-weighted images and hyperintense on T1-weighted images. It shows annular enhancement following intravenous contrast administration, with slight nodularity at its inner margin, and perilesional vasogenic edema with mild collapse of the posterior horn of the ipsilateral lateral ventricle. It measures approximately 16 × 12 mm. A lesion of likely infectious origin is suspected (Figure. 2).

A biopsy of the lesion was performed, obtaining a histopathological diagnosis of diffuse high-grade glioma, pediatric-type, IDH-wildtype, H3-wildtype, C-MYC and N-MYC amplification negative, WHO grade IV (2021) (Figure. 3).

3 Discussion

We present the clinical case of a pediatric patient diagnosed with posterior fossa medulloblastoma and a supratentorial radiation-induced tumor (high-grade glioma), diagnosed four years after radiation therapy, which presented a challenge in neuroradiological diagnosis due to its unusual characteristics.

A current challenge in neuroradiology is to establish, prior to surgical treatment, the etiology of CNS lesions in oncology patients, who, due to their underlying pathology, may present with disease recurrence, opportunistic infections, secondary tumors, and post-radiotherapy changes, among others.

It is known that radiation-induced gliomas arise in patients who have received radiation therapy for primary tumors, most frequently in those with lymphoblastic leukemia and medulloblastoma, following are typically more aggressive, with PDGFRA amplification and loss of CDKN2A/B, and are H3/IDH-negative8 , as was the second tumor diagnosed in our patient [9].

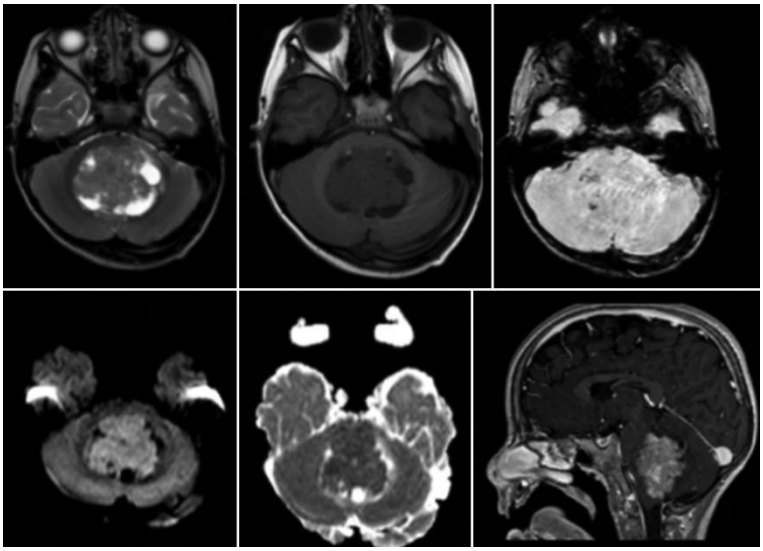

Figure 1. Predominantly solid expansive lesion with cystic/necrotic areas in the dilated fourth ventricle, with a mass effect on the periventricular cerebellar parenchyma, ventral displacement and compression of the brainstem, and collapse of the peritruncular cisterns. It exhibits iso-hypointense signal on T1 (A) and T2 (B) images, with restriction on DWI sequences (D and E), and punctate hypointense images on SWI (C), which may correspond to calcifications. Post-contrast T1-weighted sequence (F) with heterogeneous enhancement

The radiological characteristics of wild-type pediatric H3/IDH diffuse glioma are lesions with mass effect and heterogeneous, annular post-contrast enhancement; however, tumors with gene amplification may be more circumscribed, with mild perilesional edema and homogeneous enhancement following contrast administration [10,11].

It should be noted that some series assert that diffuse midline gliomas represent an atypical case among high-grade tumors with regard to their behavior on ADC, being similar to low-grade tumors [12]. These same studies suggest that DWI, together with ADC, is more useful in differentiating infratentorial tumors than supratentorial ones [2].

On the other hand, as a differential diagnosis for lesions lesions that exhibit ring-like contrast enhancement in cancer patients, such as our case, post-radiation necrosis, cerebral abscesses, and granulomatous lesions must be considered. In all of these, we can find images that present ring-shaped contrast enhancement and vasogenic edema. Using the DWI sequence, hypercellular lesions (high-grade tumors and abscesses) that show diffusion restriction can be distinguished. However, there is a small number of high-grade gliomas that exhibit ring-like enhancement with minimal restriction on DWI, particularly in intratumoral necrotic areas [1,13].

Nevertheless, it remains a challenge to differentiate, using imaging techniques, high-grade tumors that exhibit characteristics similar to low-grade lesions, as they generally present with intratumoral hemorrhages, areas of necrosis or liquefaction, pyogenic superinfection, etc.

In our case, the patient presented a lesion with sharp margins and ring-shaped enhancement, without restriction diffusion restriction and extensive perilesional edema, which led to the differential diagnosis of a granulomatous lesion.

We believe it is necessary to continue developing and refining new MRI techniques to provide an accurate diagnosis prior to surgical intervention, especially in the pediatric oncology population.

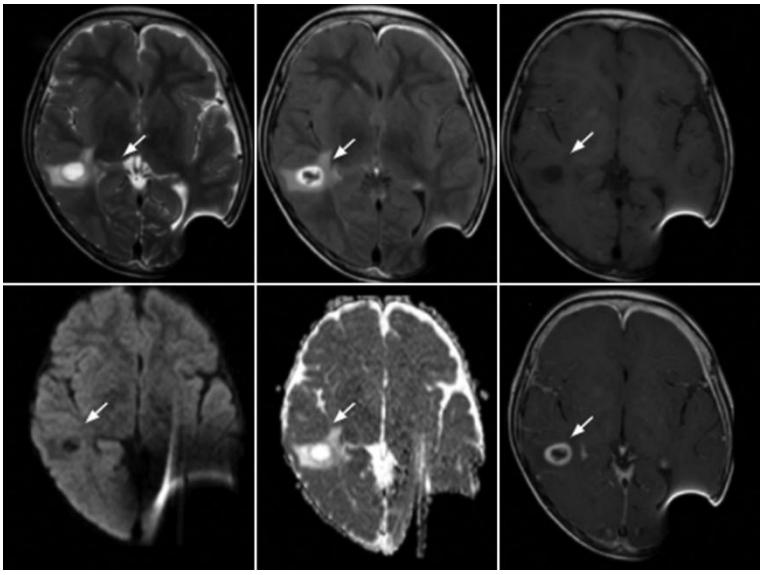

Figure 2. Follow-up MRI six years after resection of the primary lesion, showing a focal lesion in the right posterior temporal white matter, whose wall is subtly hypointense on T2-weighted imaging (A) and hyperintense on T1-weighted imaging (B), and (C) the center shows signal isointense to CSF with no diffusion restriction (D and E). It demonstrates ring enhancement after intravenous contrast administration (F), with slight nodularity on its inner margin

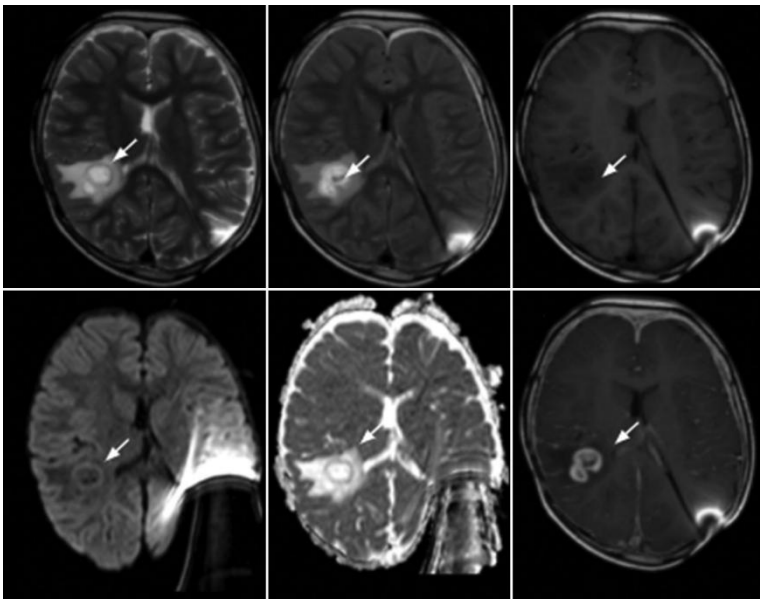

Figure 3. Follow-up MRI three months after the last follow-up, showing progression with greater confluence of T2(A)-FLAIR signal abnormalities (A and B) in the right posterior temporal parenchyma, currently with a cystic lesion showing thickened, irregular, hyperintense margins on T1 (C) with mild diffusion restriction of the wall (D and E) and ring enhancement after intravenous contrast (F)

Ethical responsibilities

Protection of humans and animals. The authors declare that no experiments were conducted on humans or animals for this research.

Data confidentiality. The authors declare that they have followed their institution's protocols regarding the publication of patient data.

Right to privacy and informed consent. The authors have obtained informed consent from the parents of the patient referred to in the article. This document is in the possession of the corresponding author.

Use of artificial intelligence to generate texts. The authors declare that they have not used any type of generative artificial intelligence in the writing of this manuscript nor for the creation of figures, graphs, tables, or their corresponding footnotes or legends.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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