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Case Report

Dysembryoplastic Neuroepithelial Tumor in an Atypical Location without Epilepsy: A Case Report

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Abstract

Dysembryoplastic neuroepithelial tumors (DNTs) are low-grade mixed glioneuronal tumors. They are rare tumors mostly located in the cerebral cortex, particularly in the temporal lobe, and are associated with intractable complex partial seizures in young patients. Here, we present the case of an 8-year-old child with upper left and external strabismus with a challenging pathological diagnosis. Magnetic resonance imaging (MRI) revealed a tumor expanding into the midbrain, right thalamus, and right medial temporal lobe. The tumor was predominantly located in the white matter and infiltrated the cortex of the right medial temporal lobe. Based on the patient's profile, neurological symptoms, and neuroradiological findings, the tumor was interpreted as a possible diffuse midline glioma. Surgery was performed, and the right temporal lobe, mainly the white matter containing the medial cortex, was resected. Morphological features of DNT, such as floating neurons, were present only in the cortex at the edge of the resected tumor and were difficult to distinguish. In this case, DNT presented with atypical radiological and symptomatic findings, making the pathological diagnosis of a lesion with infiltration of the cortex uncertain. This study advocates a multidisciplinary diagnostic procedure for atypical radiological and symptomatic DNT findings.

Keywords: DNA Methylation Profiling; Dysembryoplastic Neuroepithelial Tumor; White Matter Tumor

Introduction

Dysembryoplastic neuroepithelial tumors (DNTs) are rare benign mixed glioneuronal tumors occurring in children and young adults [1,2]. In 2021, the World Health Organization categorized DNTs as grade 1 cortical glioneuronal tumour [3]. The most common presentation of a DNT is focal epilepsy, which is often resistant to antiepileptic drugs. DNTs are primarily located in the supratentorial cortex. Over 67% of cases are located in the temporal lobe, with preferential involvement of mesial structures [4]. The multinodular architecture of the lesion and the accompanying presence of "floating neurons" are the most distinctive morphological features of DNT. Here, we describe a case of DNT presenting with atypical radiological and symptomatic findings, making the pathological diagnosis as a lesion with infiltration of the cortex uncertain. We emphasize the importance of an integrated approach for the accurate diagnosis an atypical case.

Case Presentation

The patient was 8-year-old child with upper left and external strabismus. Magnetic resonance imaging (MRI) revealed a tumor expanding into the midbrain, right thalamus, and right medial temporal lobe (Figure 1 A). The diameter of the tumor was 55 mm. The tumor was predominantly located in the white matter and infiltrated the cortex of the right medial temporal lobe. The patient presented with eye movement disorder but no seizures. Based on the patient's profile, neurological symptoms, and neuroradiological findings, the tumor was interpreted as a possible diffuse midline glioma.

The right temporal lobe, mainly the white matter containing the medial cortex, was surgically resected (Figure 1B). Pathological analysis revealed ruled out diffuse midline glioma, and a provisional diagnosis of pediatric-type diffuse low-grade glioma, not otherwise specified (NOS) was made. We consulted the National Center for Child Health and Development for the pathological diagnosis. The tumor tissue was mainly located in white matter and partial cortex. Details of the cortical tissue were re-examined. Distinct morphological features of DNT were identified in the cortical lesion, and a definitive diagnosis was obtained. One and a half years after the operation, the patient was stable and had no worsening neurological status. Residual tumor was observed without recurrence.

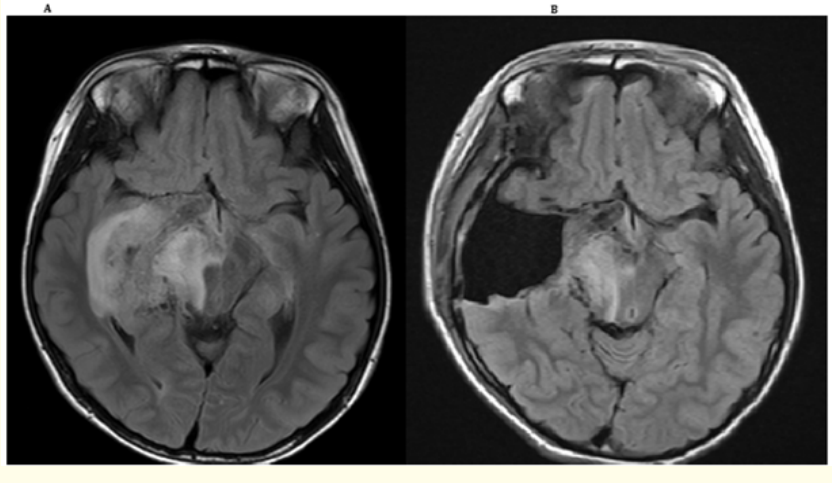

Figure 1: A. Magnetic resonance imaging (MRI) revealed a tumor expanding into the midbrain, right thalamus, and right medial temporal lobe.

B. The tumor tissue was mainly resected for white matter and partial cortex.

Pathological findings

Hematoxylin-eosin staining revealed diffuse proliferation of oligodendroglia-like cells with round nuclei. Some nodules contained a mucoid substance and were lined with oligodendroglia-like cells (Figure 2 A and B). No mitotic figures, tumor necrosis, or microvascular proliferation were observed. Immunohistochemical analyses revealed that the tumor cells were positive for Olig2 and negative for GFAP, IDH1R132H, and H3K27M. ATRX was retained. The MIB-1 labeling index was 1.3%.

Diffuse midline glioma was ruled out, and the provisional diagnosis was pediatric- type diffuse low-grade glioma, NOS. We consulted the National Center for Child Health and Development on pathological diagnosis. The tissue details were re-examined. The tumor mainly consisted of white matter and partial cortex tissues. Hematoxylin-eosin staining of the cortex lesion revealed an oligodendroglia-like morphology accompanied by a mucoid matrix, with a small number of floating neurons that were positive for NeuN (Figure 3).

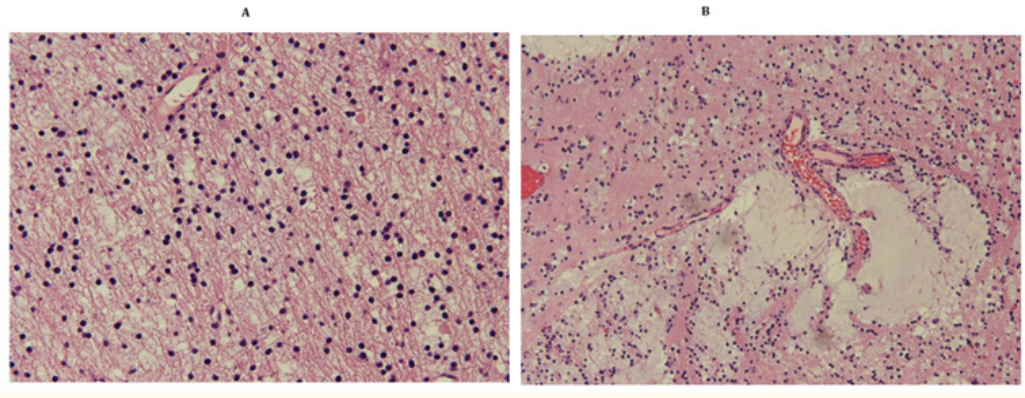

Figure 2: A.Hematoxylin-eosin staining revealed oligodendroglia-like cells with diffuse round nuclei. B.Some areas with a mucoid substance were lined with oligodendroglia-like cells.

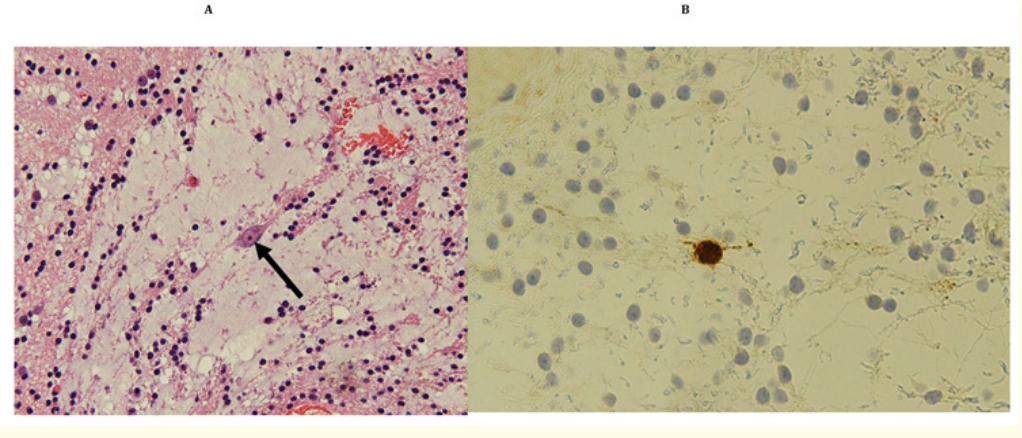

Figure 3: A.Hematoxylin-eosin staining of the cortex revealed an oligodendroglia-like morphology accompanied by a mucoid matrix and a floating neuron. Arrow: a floating neuron
B. A floating neuron that was positive for NeuN.

Genetic findings

Genetic analysis of surgical specimens using pyrosequencing was performed for IDH1R132, IDH2R172, BRAFV600, H3F3AK27, H3F3AG34, HIST1H3B, TERTC228T,FGFR1N546, and FGFR1K656; no hotspot mutations were detected. The final diagnosis was DNT, taking into consideration the morphological findings.

DNA-methylation profiling was performed at the DKFZ Genomics and Proteomics Core Facility (Heidelberg, Germany) utilizing the Illumina HumanMethylation450 BeadChip array (450 k array or EPIC) (Illumina, San Diego, USA) according to the manufacturer's instructions and as previously reported [5]. The methylation profile, integrated with the few specific glioneuronal elements in pathological diagnosis and the lack of genetic alterations, supported a diagnosis of the tumor as DNT (supplementary Figure 1).

Version 12.8 of the brain classifier results (12.8)

Methylation classes (Highest level >= 0.3, lower levels >= 0.1, all of lowest level)	Calibrated score	Interpretation	
Low Grade Glial/glioneuronal/neuroepithelial Tumours	0.97	match	✓
Low Grade Glioneuronal Tumour	0.96	match	✓
Dysembryoplastic Neuroepithelial Tumour	0.92	match	✓
Mc Dysembryoplastic Neuroepithelial Tumour	0.92	match	✓

Legend: ✓ Match (score >= 0.9) ✗ No match (score < 0.9): possibly still relevant for low tumor content and low DNA quality cases.

Supplementary Figure 1: Methylation profiling report.

Discussion

DNT is a rare and benign supratentorial mixed glioneuronal tumors characterized by its intracortical location, multinodular architecture, and heterogeneous cellular composition [1,2]. It occurs in young patients with medically intractable epileptic seizures [1,2]. DNTs develop in the cerebral cortex, with the temporal lobe being the most common location, although some parts of the cerebral cortex may also be involved [6]. Only a handful of cases have been reported as having arisen at other sites, including the cerebellum [7,8], cerebellum and brainstem [9], and caudate nucleus [10]. DNTs commonly range between 10–25 mm in size, although occasionally larger tumors up to 70 mm have been reported [11]. Particularly rare are more sizable lesions involving not only a temporal lobe but the hypothalamus and basal ganglia as well [12]. Grossly, tumors appear as well-defined solitary nodular masses or poorly demarcated lesions. Most tumors are located cortically in the cut section and may extend into the underlying subcortical white matter of larger tumors [11]. We report an unusual case in which a DNT was located predominantly in the white matter of the brainstem, right thalamus, and medial temporal lobe; infiltrated the cortex in the temporal lobe; and spread extensively. The most common presentation of DNTs is focal epilepsy, which is often resistant to antiepileptic drugs. Our patient, with a tumor in an uncommon location, presented with eye movement disorder but no epilepsy. The patient presented atypical symptoms that were difficult to distinguish.

DNT cases are characterized by intracortical nodules with a columnar architecture of uniform oligodendrocyte-like cells within a microcystic background [13]. They are typically oriented perpendicularly to the cortical/pial surface [13], with large neurons scattered within microcystic areas, sometimes making an impression that they "float" in the mucin-filled background. The multinodular architecture of the lesion accompanied by the presence of "floating neurons" are the most distinctive morphological features of DNTs. The non-specific and diffuse forms of DNT may histologically resemble those of glioma, ganglioglioma, pilocytic astrocytoma, and diffuse astrocytoma. Due to cellular heterogeneity, biopsy specimens or incomplete resection of a DNT may lead to an erroneous diagnosis of focal cellular dysplasia or low-grade glioma, depending on which part of the tumor is sampled [14]. In our case, besides nonspecific symptoms, the tumor occurred mainly in the white matter, a non-specific location for DNT, and morphological features of DNT, such as floating neurons, were present only in the cortex at the edge of the resected tumor, making it difficult to identify distinctive features (confirmed on review) [15,16].

However, there have been reported cases of DNTs in uncommon locations such as the cerebellum, pons, and caudate nucleus area, and a pathological diagnosis was obtained even if the lesion was not in the cortex [9,10,7,17,12]. We need to pay attention that tumors with an uncommon location, such as in our case, may not be diagnosed appropriately.

Successful diagnosis of DNT, a benign tumor, is important because it precludes unnecessary radiotherapy and chemotherapy in young patients. The genomic profile of DNTs has been reported, and *FGFR1* alterations and *BRAF* V600E mutations characterize DNTs. Internal tandem duplication of the tyrosine kinase domain of *FGFR1* is the most prevalent genetic abnormality, seen in 40–60% of DNT cases, followed by missense mutations in *FGFR1* [4]. *BRA*F V600E mutations are observed in approximately 50% of DNTs [4]. Our patient lacked the most prevalent genetic abnormalities of DNTs. A diagnosis of DNT cannot rely solely on imaging features and neurological symptoms but rather requires a multidisciplinary approach, including morphological pathology and molecular analyses such as methylation profiling, to reach a definitive diagnosis [18,19].

Conclusion

This report describes a patient with a DNT who presented with atypical radiological and symptomatic findings, making the pathological diagnosis of the lesion uncertain. This study advocates a multidisciplinary diagnostic approach for atypical radiological and symptomatic DNT findings.

The methylation profile, integrated with the few specific glioneuronal elements in pathological diagnosis and the lack of genetic alterations, supported a diagnosis of the tumor as DNT.

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Conflict of interest

The authors declare no conflict of interest.

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