Dysembryoplastic neuroepithelial tumor-like pilocytic astrocytoma
A case report

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Abstract

Rationale: Pilocytic astrocytoma (PA) typically shows biphasic pattern with a mixture of loose microcystic and compact regions, in which it is not uncommon to see heterogeneous morphology. However, there has not been reported in the literatures of the PA type which shows similarity to dysembryoplastic neuroepithelial tumor (DNT) in both histological morphology and immunophenotype.

Patient concerns: The present study described a case of PA affecting the right temporal-occipital lobe in a 22-year-old male patient. Morphologically, it composed of totally distinctive microcystic pattern. The classical biphasic pattern of PA was not observed. Immunohistochemically, neuronal marker NeuN was expressed in tumor cells scattered in the background which simulated its expression morphology in DNT. However, KIAA1549-BRAF fusion gene was identified by fluorescence in situ hybridization (FISH), supporting for the diagnosis of PA.

Diagnoses: DNT-like PA (WHO grade I).

Interventions: The tumor was totally removed via a right temporal-occipital craniotomy.

Outcomes: The patient is free of local recurrence and dissemination eleven months after surgical resection of the lesion.

Lessons: We herein report a rare case of DNT-like PA. For diagnosis, KIAA1549-BRAF fusion gene should be detected under similar situation.

Abbreviations: DNT = dysembryoplastic neuroepithelial tumor, FISH = fluorescence in situ hybridization, GFAP = glial fibrillary acidic protein, GG = ganglioglioma, IDH1 = isocitrate dehydrogenase 1, MRI = magnetic resonance imaging, NF1 = neurofibromatosis type 1, Olig2 = oligodendrocyte transcription factor 2, PA = pilocytic astrocytoma, PXA = pleomorphic xanthoastrocytoma.

Keywords: dysembryoplastic neuroepithelial tumor, fluorescence in situ hybridisation, KIAA1549-BRAF fusion gene, pilocytic astrocytoma

1. Introduction

Pilocytic astrocytoma (PA) is a common World Health Organization (WHO) grade I glioma occurring in children and adolescents. Most PAs show benign clinical behavior and favorable prognosis. But in a small subset of patients, they may behave aggressively.[1,2] Under the microscopy, besides classical biphasic architecture, morphological heterogeneity may be found in PAs, which simulates the characteristics of the other low-grade glial neoplasms, such as oligodendroglioma, pleomorphic xanthoastrocytoma (PXA), ependymoma, and diffuse astrocytoma.[3] However, PAs that are histopathologically similar to dysembryoplastic neuroepithelial tumors (DNTs) in both histological morphology and immunophenotype have not been reported before. We herein showed a DNT-like PA case, which expanded the morphological profile of PA.

2. Case report

A 22-year-old male visited local hospital due to a car accident in November 2016. CT scans detected a mass located in the right temporal-occipital lobe. The patient refused to do any treatment because of no clinical symptoms at that time. Two months later, he presented with a focal epilepsy, which was improved after having anti-epileptic drugs. In February 2017, he was referred to our hospital (Southern District of Anhui Provincial Hospital) because of deteriorating symptom. Magnetic resonance imaging (MRI) examination revealed a 1.1 × 1 cm round homogenous mass, which was hyperintense on T2 (Fig. 1A) and slightly hypointense on T1 weighted images (Fig. 1B) without gadolinium enhancement (Fig. 1C). The patient denied having any family history of neurofibromatosis type 1 (NF1) and no associated symptoms were found during the previous physical examinations. The lesion was totally removed via a right temporal-occipital craniotomy. Intraoperatively, the lesion was well...
case report. Consent was provided by the patient for the publication of this not relate to any human trials or the patient (Fig. 3). The DNT (Fig. 2F). To confirm the diagnosis, further assay with fluorescence in situ hybridization (FISH) was applied and KIAA1549–BRAF fusion gene was found in the tumor (Fig. 2). The Ki67 labeling index was <1% (Fig. 2E). Confusingly, neuronal marker NeuN was expressed in tumor cells scattered in the background which normally found in PAs. The Ki67 labeling index was <1% (Fig. 2E). Confusingly, neuronal marker NeuN was expressed in tumor cells scattered in the background which normally found in DNT (Fig. 2F). To confirm the diagnosis, further assay with fluorescence in situ hybridization (FISH) was applied and KIAA1549–BRAF fusion gene was found in the tumor (Fig. 2). The final diagnosis was DNT-like PA (WHO grade I).

Ethical approval was not required for this case report as it did not relate to any human trials or the patient’s privacies. Informed consent was provided by the patient for the publication of this case report.

3. Discussion

PA is a clinicopathological heterogeneous WHO grade I tumor.[3,4] Clinically, PAs accounts for 20% of brain tumors in the patients under 20 years old.[5] Approximately 5% to 10% PAs are associated with neurofibromatosis type I (NF1), especially those cases which arise in the optic/Chiasmal region.[6] PAs mainly involve the neuraxis, such as cerebellum, optic pathway, hypothalamus, brainstem, and spinal cord, while the supratentorial region is also frequently encountered.[3,6] Clinical manifestations of PAs are dependent on the lesion locations. Neuroradiologically, PAs typically show hypo- or iso-intense lesion on T1-weighted images with enhancement and hyperintense on T2-weighted images. Most lesions in the cerebellum are cystic accompanying with a mural enhancing nodule under MRI, while others display as infiltrative masses in the optic pathway.[7] However, just like our case, the imaging findings of the lesions can be atypical in other areas.[7]

Instead of typical contrast enhancement under MRI, they showed an atypical solid mass without cystic change and infiltration.

Histologically, PAs typically show biphasic pattern with a mixture of loose microcystic and compact regions. In the loose microcystic parts, eosinophilic granular bodies can be seen. Meanwhile, the bipolar piloid cells compose the compact areas, in which rosenthal fibres are easily detected. Occasionally, PAs exhibited a predominantly or even entirely growth pattern.[5] It is not unusual to find heterogeneous morphological characteristics in PAs, such as oligodendroglioma, PXA, ependymoma, and diffuse astrocytoma.[3] However, PAs with NeuN positive cells in entirely microcystic background which mimicked DNT was not reported in the literature before. The exact reason for this is not clear. We inferred that these NeuN positive cells may be entrapped neurons or due to unspecified immunohistochemical reactions.

In addition to clinicopathological heterogeneity, PAs also display molecular heterogeneity. Jones et al[8] firstly found the KIAA1549–BRAF fusion gene exhibited in most of the PAs. This fusion gene can activate the mitogen-activated protein kinase pathway and participant in the formation of PAs. Except PAs, KIAA1549–BRAF fusion gene can only be detected in diffuse leptomeningeal glioneuronal tumors.[4,5] Therefore, harboring KIAA1549–BRAF fusion gene contributes to the diagnosis of PAs. In our case, the detection of BRAF fusion gene was the determining factor in the distinguishing between PA and DNT. In addition to KIAA1549–BRAF, other BRAF fusion partners were also found in PAs, including FAM131B, RNF130, CLCN6, MKRN1, GNII, and GIT2.[10] Besides, activating point mutation BRAF V600E occurs in a small part of PAs, especially in the supratentorial locations,[11] whereas it is the most common finding in papillary craniopharyngiomas, PXA, gangliogliomas (GG) and DNT.[11] Moreover, aberrant DNA methylation has been studied in PAs, which varied according to tumor locations as well.[11]

From a differential diagnosis perspective, our case should be distinguished from DNT. It is well known that DNT is a type of epilepsy-associated low-grade glioneuronal tumor which typically occurs in the cerebral cortex of children and adolescents. After surgery, the recurrence and progression of DNTs are exceptional. Their histological features are multinodular with glioneuronal elements, which contain oligodendrocyte-like cells attached to bundles of axons and neurons with normal cytology floating in a...
myxoid interstitial fluid. In rare cases, DNTs in the septum pellucidum or the supratentorial midline may be misdiagnosed as glioma, while astrocytoma with microcystic change and oligodendrocyte-like cells is hard to distinguish from DNT. In our case, both histological morphology and immunophenotype are similar to DNT, molecular detection was the only way to distinguish between PA and DNT. 30% of DNTs harbor BRAF V600E mutation, while KIAA1549–BRAF fusion gene has never been detected in DNT. Therefore, the detection of BRAF fusion gene supports the diagnosis of PA. However, it is important to note that DNT can coexist with PA and the recurrent DNT may display the morphology of PA. Besides, our case also needs to differentiate from other histologic mimics, including GG, oligodendroglioma and extraventricular neurocytoma. GG is another type of epilepsy-associated low-grade glioneuronal tumor which contains NeuN positive neuronal and GFAP positive glial cell elements. But loose microcystic regions were not easy to see in GG. BRAF V600E mutation occurred in 35% GG. However, there has no BRAF fusion been detected in GG. It is not uncommon to see oligodendrocyte-like cells in PAs, resulting in some overlapping features with oligodendroglioma or extraventricular neurocytoma. However, oligodendroglioma frequently demon-
strates IDH mutation and 1p/19q codeletion,\[4\] while extraventricular neurocytoma diffuse expresses neuronal marker.\[21\] Both of them have no BRAF fusion.

As a WHO grade I glioma, PAs generally have favorable prognosis. The 10-year survival rate is over 95% after operation.\[3\] Spontaneous regression may be encountered in PAs, especially in patients with neurofibromatosis type 1.\[1,2\] A small minority of PAs may recur after surgery or disseminate to the leptomeninges.\[1,2\] Surgical resection is the first treatment choice for patients with PAs, and radiotherapy or chemotherapy is applied to patients who are inoperable, subtotally resected, or progressive.\[5\] Eleven months after the operation, our case showed no local recurrence and dissemination.

PAs are heterogeneous tumors in histological morphology, immunophenotype and molecular characteristics. We report here a case of PA that both histological morphology and immunophenotype are similar to DNT, which expanded the morphological profile of PA. Therefore, we suggest that KIAA1549–BRAF fusion gene status should be assessed under similar situation to confirm the diagnosis.

**Author contributions**

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