

# Cerebral astroblastoma with oligodendroglial-like cells: A case report

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## Case Report

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# Abstract

**Background:** Astroblastoma is a rare tumor of the central nervous system, with unclear biological behavior and origin. Its histopathological features have been well established. However, to the best of our knowledge, astroblastoma with oligodendroglial-like cells have not been reported.

**Case presentation:** Herein, we reported a case of astroblastoma with atypical pathological features. A 15-year-old girl presented with nausea, vomiting, headache and visual disturbance. Magnetic resonance imaging (MRI) revealed a large neoplasm in the left temporal lobe. Histologically, the tumor showed solid and pseudopapillary structure. The tumor cells were radially arranged around blood vessels, with a single, prominent process, and as astroblastic pseudorosettes. More importantly, typical oligodendroglial-like cells were observed. In addition to membrane staining for EMA, immunohistochemical staining also showed that the tumor cells were positive for GFAP and Vimentin. The oligodendroglial-like cells were positive for GFAP, Vimentin, and Olig-2. The Ki-67 labeling index was about 4%. Sequencing for IDH1 codon 132 and IDH2 codon 172 gene mutations showed negative results. Furthermore, fluorescent analysis revealed neither 1p nor 19q deletion in the lesion. Based on these findings, the tumor was finally diagnosed as astroblastoma.

**Conclusions:** Herein, we reported an extremely rare case of astroblastoma, which was morphologically characterized by the appearance of oligodendroglial-like cells.

## Introduction

According to the 2016 edition of the World Health Organization (WHO) Classification of Tumors of the Central Nervous System [1], astroblastoma belongs to the “other glioma” category. It can occur at any age, but is more common in children and young adults [2, 3]. Astroblastoma usually develops in cerebral hemispheres, but is also found in other parts of the nervous system [4]. On imaging examination, astroblastomas are well-demarcated masses [5]. Although the microscopic description of astroblastoma in the existing literature is not completely consistent, there are two well established characteristics: 1. The perivascular pseudorosette of tumor cells with short and stout cytoplasmic processes, radiating towards central blood vessels that often demonstrate sclerosis. 2. Expression of glial fibrillary acidic protein (GFAP) [6, 7]. Herein, we reported an extremely rare case of astroblastoma accompanied by oligodendroglial-like cells.

## Case Presentation

A 15-year-old Chinese female presented with nausea, vomiting and vertigo for one year. Her symptoms gradually worsened, with headache and hypopsia for one month. Magnetic resonance imaging (MRI) revealed a large, well-circumscribed, 7.5 × 5.0 × 5.0 cm size cystic-solid lesion in the left temporal lobe. The tumor appeared hyperintense on T1 and T2-weighted images. The signal in most cystic parts of the tumor was uniform, but the solid part was uneven. The tumor compressed the left ventricles and lateral

fissure cistern, and the midline structure was shifted to the right (Fig. 1). Radiological diagnosis was 'other astrocytic tumor, pilocytic astrocytoma or pleomorphic xanthoastrocytoma'. A craniotomy with total excision of the tumor was performed. The present patient did not undergo chemotherapy or radiotherapy after surgery, only supportive treatment. And she had no abnormality after retesting so far.

## Materials And Methods

The resected specimens were fixed with 10% neutral-buffered formalin and embedded in paraffin blocks. Tissue blocks were cut into 4  $\mu$ m slices, deparaffinized in xylene, rehydrated with graded alcohols, and immunostained with the following antibodies: cytokeratin (CK), glial fibrillary acidic protein (GFAP), mutant IDH1 R132H, S-100, Vimentin, synaptophysin (Syn), oligodendrocyte transcription factor 2 (Olig-2), alpha-Thalassemia/mental retardation syndrome X (ATRX), neuronal nuclear antigen (NeuN), p53 and Ki67 (MaiXin, China). Then, the sections of each specimen were stained with streptavidin–peroxidase (KIT-9720, Ultrasensitive TM S-P, MaiXin, China) according to the manufacturer's instructions. The chromogen used was diaminobenzidine tetrahydrochloride substrate (DAB kit, MaiXin, China). All samples were mildly counterstained with hematoxylin, dehydrated and mounted. For the negative controls, each sample was incubated with PBS instead of the primary antibody, as described above.

Fluorescent in situ hybridization (FISH) was performed to check for deletions of chromosomes 1p and 19q. Dual color-probe hybridization was performed with Vysis 1p36/1q25 and 19q13/19p13 FISH probe kit (Abbott Molecular, Illinois, USA) according to the manufacturer's instructions. At least 100 non-overlapping nuclei were counted; samples were considered to be 1p or 19q-deleted when > 30% of counted nuclei presented one target (red) signal and two reference (green) signals. Sanger sequencing was used to detect the mutations of IDH 1 and 2 genes.

## Results

Small grayish-red fragments of the resected lesion were sent for histological examination. Histological examination showed that the lesion had two patterns in different proportions, astroblastoma area and oligodendroglial-like cells area, with a clear boundary between them (Fig. 2A). The astroblastoma area was composed of poorly cohesive tumor cells forming solid or pseudopapillary structure (Fig. 2B). Importantly, elongated tumor cells with broad footplates were found clustered around blood vessels forming astroblastic pseudorosettes. These cells were often polarized, with the nucleus on one end and a tail-like cytoplasmic process on the other end. Moreover, they possessed abundant eosinophils in the cytoplasm, and mitosis was rare (Fig. 2C). The tumor tissue showed no necrosis or calcification. Blood vessels showed no endothelial cell hyperplasia or hyalinization. Notably, oligodendroglial-like cells with clear cytoplasm, perinuclear halos and round nuclei were observed in a specific area, which showed oligodendroglial-like honeycomb appearance, and the mitosis rate was typically low (Fig. 2D).

Immunohistochemical staining showed that the astroblastoma cells were negative for IDH1 R132H (Fig. 3A), CK, NeuN, Syn, p53 and Olig-2, but positive for Vimentin, S-100 and ATRX. GFAP was strongly

positive in the cytoplasm of tumor cells (Fig. 3B). Some tumor cells were positive for EMA on the cell membrane (Fig. 3C). The oligodendroglial-like cells were positive for Olig-2 and GFAP, but negative for IDH1 R132H, EMA, NeuN, p53 and Syn. The Ki-67 proliferation index was about 4%. There were no IDH1/2 mutations in the tumor. FISH analysis revealed no 1p and 19q deletions in the lesion. Based on these findings, the tumor was diagnosed as astroblastoma with oligodendroglial-like cells.

## Discussion

Astroblastoma is a rare glial neoplasm, which was not initially recognized. Even after astroblastoma was first reported by Bailey and Cushing, its existence and origin remained controversial [8]. Based on microscopy observation, astroblastoma was initially classified as a transitional type between the astrocytoma and the glioblastoma multiform [9]. Some scientists believed that GFAP and vimentin positivity in astroblastoma supported the hypothesis that this tumor was derived from the cytogenetically more primitive astroblast [10, 11], or arose from a process of dedifferentiation involving mature astroglial cells [12]. However, an ependymal or tanycyte-derived origin of astroblastoma is considered by many authors based on the electron microscopic features [13, 14]. Tanycytes are suggested to be glial precursor cells that may occur during normal human embryogenesis, which explains the existence of congenital astroblastoma [15, 16]. Astroblastoma is often mixed with other types of tumor cells such as glioblastomas or anaplastic astrocytomas, and the pseudo-chrysanthemum cluster structure also appears in other tumors, leading to controversy about its existence [17].

With the advancement of gene identification technology, numerous specific genes have been identified in astroblastomas. The most frequent gene alterations detected were MN1 mutation, gain of chromosome arm 20q and chromosome 19, loss of 9q, 10 and X [18–20]. These findings suggested that astroblastomas represent a distinct entity with characteristic cytogenetic features that differ from those of ependymomas and astrocytomas. Because large sample gene detection studies have not been conducted for astroblastomas, there is no unified gene mutation spectrum. Moreover, tumors with histological features of astroblastoma may result from diverse and possibly distinct genetic events [21].

Perivascular pseudorosettes are also found in other tumors. So the histological differential diagnoses of astroblastomas include ependymomas and papillary meningiomas. The astroblastoma in our patient exhibited broad footplates as opposed to the tapering processes seen in ependymoma. Moreover, in contrast to ependymomas, the spaces between the pseudorosettes were often rarified. EMA expression was previously shown to be typically localized at the cell membrane in astroblastomas [22–24], which was also observed in our patient. In ependymoma, EMA is expressed along the luminal surface of some ependymal rosettes or manifests as dot-like perinuclear or ring-like cytoplasmic structures [25]. Therefore, we ruled out the diagnosis of ependymoma based on morphology and immunohistochemistry. The distinction between astroblastomas and papillary meningiomas is aided by immunohistochemical features such as positive GFAP staining in astroblastomas. Interestingly, the oligodendrocyte-like cells were outside the papillary areas in our patient, with clear boundaries in between. Meanwhile, neither IDH

1/2 mutation nor 1p/19q co-deletion was observed, so the diagnosis of oligodendroglioma was ruled out. Based on these findings, the tumor was diagnosed as astroblastoma with oligodendroglial-like cells.

Oligodendroglial-like cells can appear in many central nervous system tumors, such as dysembryoplastic neuroepithelial tumor (DNT) [26], rosette-forming glioneuronal tumor (RGNT) [27], papillary glioneuronal tumor [28], diffuse leptomeningeal glioneuronal tumor [29], and gangliogliomas (GGs) [30]. There is only one previous report by Lehman NL and Hattab EM that found scattered oligodendroglial-like cells between astrocytoma cells, which is different from our patient [31].

Different terminologies have been previously used to describe oligodendroglial abnormalities including oligodendroglial hyperplasia [32], clusters of oligodendroglioma [33], oligodendroglial hamartoma [34], and oligodendroglial-like cells. These lesions may represent a spectrum of the same abnormality. However, the appearance of oligodendroglial-like cells under the microscope was not the same, visible oligodendroglial-like cells floated in the mucus-like matrix, or infiltrated the tumor tissue, or were arranged in bundles. Oligodendroglial-like cells and oligodendroglioma have different gene mutation spectra. Despite oligodendroglial-like morphology, oligodendroglial-like cells do not have chromosome 1p and 19q deletions or IDH1 mutation [35]. Our patient did not have IDH1/2 mutation, or 1p and 19q deletions. Moreover, there was a clear boundary between the tumor tissue and oligodendroglial-like cells. Hence, we hypothesized that the oligodendroglial-like cells in this case were not oligodendroglioma components, but oligodendroglial-like cell hyperplasia.

## Conclusions

Herein, we described an extremely rare case of astroblastoma with oligodendroglial-like cells.

## Abbreviations

MRI	Magnetic resonance imaging
WHO	World Health Organization
CK	Cytokeratin
GFAP	Glial fibrillary acidic protein
S-100	Soluble protein-100
Syn	Synaptophysin
Olig-2	Oligodendrocyte transcription factor 2
ATRX	Alpha-Thalassemia/mental retardation syndrome X
NeuN	Neuronal nuclear antigen
P53	Tumor protein 53
Ki67	Antigen KI67
MN1	Meningioma 1
DNT	Dysembryoplastic neuroepithelial tumor
RGNT	Rosette-forming glioneuronal tumor
GGs	Gangliogliomas
FISH	Fluorescent in situ hybridization

## Declarations

### Ethics approval and consent to participate

This case study was approved by the Institutional Ethics Committee of China Medical University, Shenyang Province, China.

### Consent for publication

Written informed consent was obtained from the patient for the publication of this case report and any accompanying images. A copy of the consent form is available for review by the Editor of Diagnostic Pathology.

### Availability of data and materials

All data generated or analyzed during this case are included within the article

### Competing interests

The authors declare no conflict of interest.

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## Authors' contributions

GJ collected the clinical data and drafted the manuscript. XHT and LQC made the pathological diagnosis. QXS and WEH offered assistance in image selection. YJH made revision to the final manuscript and provided the funding support. All authors read and approved the final manuscript.

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## Figures

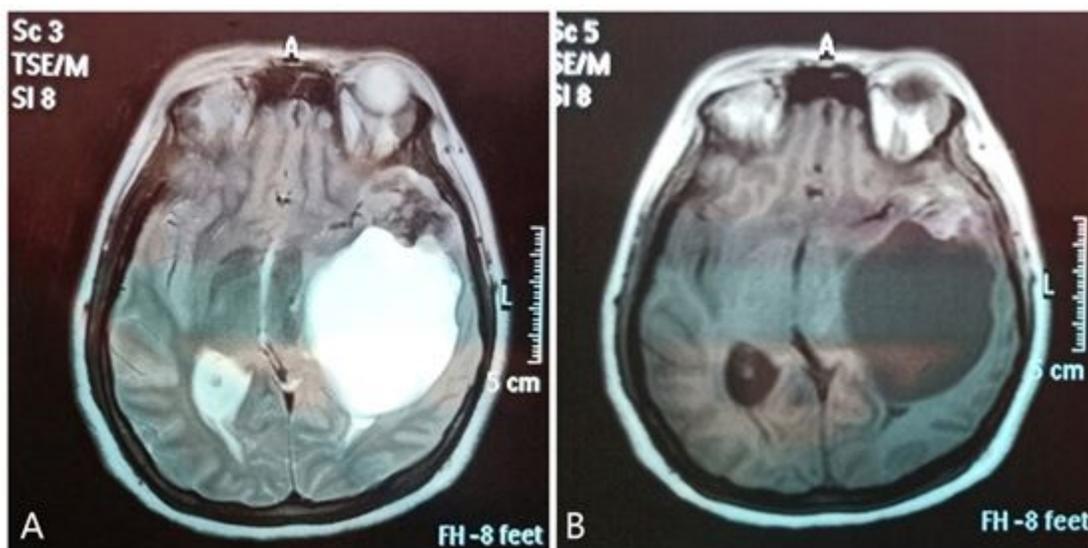
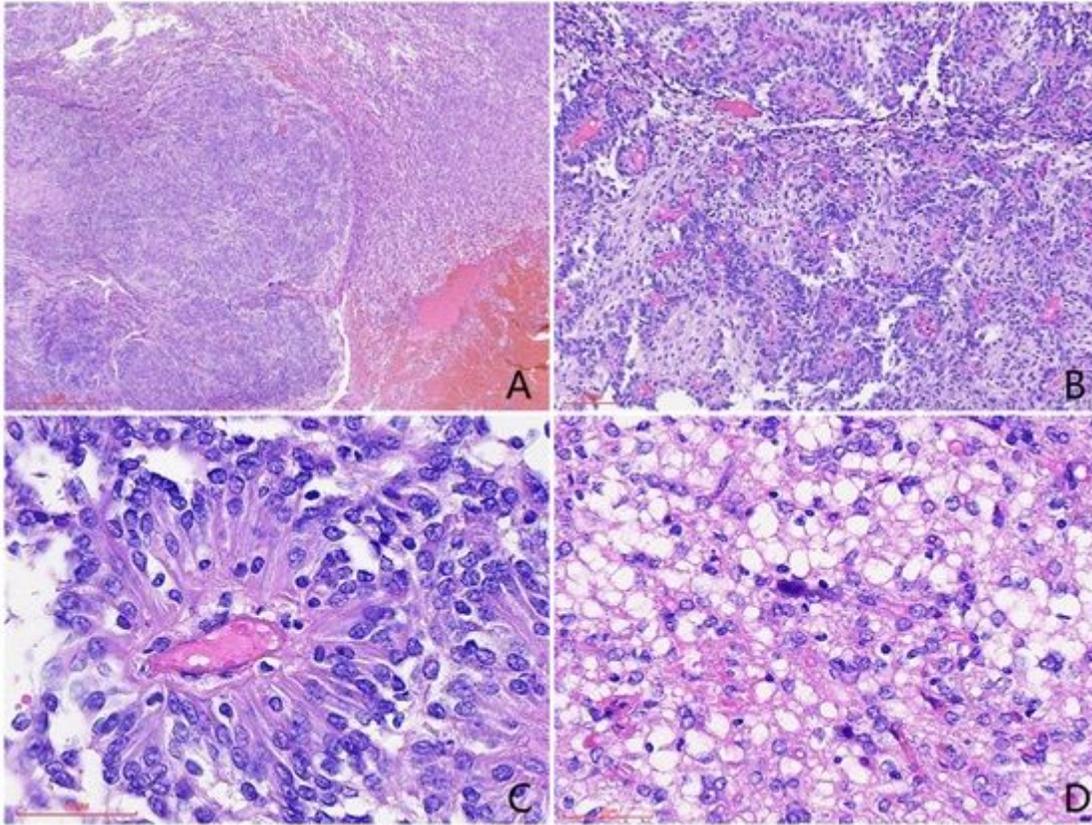


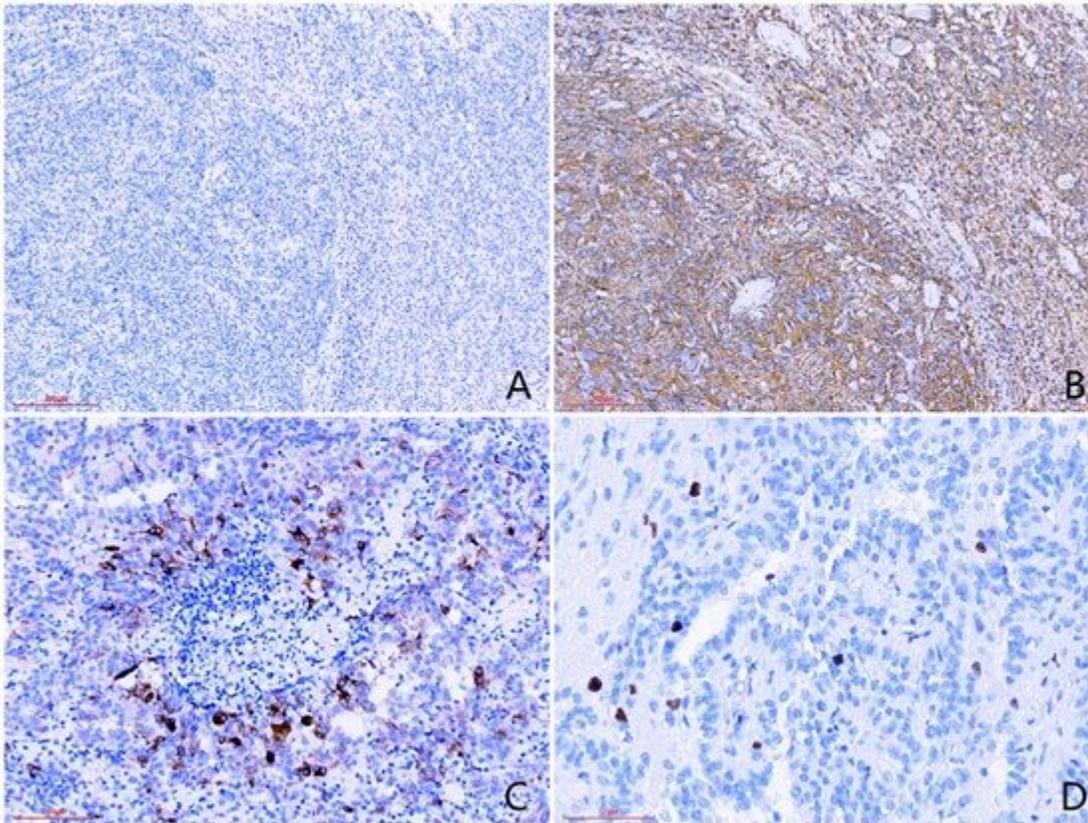
Figure 1

MRI showing a 7.5×5.0×5.0 cm size cystic-solid mass in the left temporal lobe. Cystic part of the tumor showed uniformly long T1 and T2 signals, with smooth edge. The solid part of the tumor showed irregular edge and heterogeneous signal, which was slightly hypointense on T1-weighted images and slightly hyperintense on T2-weighted images. There was no edema signal around the tumor. Tumor occupying effect was obvious, the left ventricle and lateral fissure pool were narrow, compressed and partially invisible. The midline structure was shifted to the right. There was no abnormality in the inner table of the adjacent skull. A: Axial T1-weighted image. B: Axial T2-weighted image.



**Figure 2**

Histopathological findings. (A) Border between astroblastoma and oligodendroglial-like cells was well defined. (B) The tumor was composed of poorly cohesive tumor cells forming solid or pseudopapillary structure. (C) Astroblastoma area: stout processes extended to the central vessels, forming astroblastic pseudorosettes. (D) Oligodendroglial-like cells area: the tumor cells showed a clear perinuclear halo with delicate “chicken-wire” network of branching capillaries and microcalcification.



**Figure 3**

Immunohistochemistry findings. (A) The tumor cells were negative for IDH1 R132H. (B) The tumor cells and the peripheral oligodendroglial-like cells were positive for GFAP. (C) The tumor cells showed membrane staining for EMA. (D) The Ki-67 proliferation index was about 4%.

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