Clinical Case Report

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Supratentorial intracerebral cerebellar liponeurocytoma

A case report and literature review

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Abstract

Rationale: Cerebellar liponeurocytoma is a rare tumor of the central nervous system (CNS) characterized by low proliferation but high likelihood of recurrence. Because of its rarity and the paucity of systematic follow-up, the biological behaviors and clinical features of this tumor are still poorly understood. We herein reported a case of cerebellar liponeurocytoma originating in the cerebral hemisphere.

Patient concerns: A 11-year-old male with intermittent headache, nausea, and vomiting. The first computed tomography revealed a large mass in the right cerebral hemisphere. He was transferred to our institution for neurosurgical treatment.

Diagnosis: Magnetic resonance imaging showed a large cystic—solid mass in the right frontal lobe with obvious contrast enhancement. Histopathological examinations showed sheets of isomorphic small neoplastic cells with clear cytoplasm and focal lipomatous differentiation. On immunohistochemistry, tumor cells were positive for synaptophysin, microtubule-associated protein 2, and neuronal nuclei antigen.

Interventions: The patient was performed a right fronto-parietal craniotomy, and gross total resection of the tumor was achieved without adjuvant therapy.

Outcomes: No clinical or neuroradiological evidence of recurrence or residual of the tumor was found 6 years and 2 months after initial surgery.

Lessons: Cerebellar liponeurocytoma developing in supratentorial cerebral hemisphere was first reported in the present study. The radiological and histopathological features may be useful in differentiating this rare tumor from other tumors at similar locations. A change in the nomenclature of cerebellar liponeurocytomas should be considered in future World Health Organization (WHO) classifications.

Abbreviations: cDNA = complementary DNA, CNS = central nervous system, CT = computed tomography, GFAP = glial fibrillary acid protein, H&E = hematoxylin and eosin, MAP-2 = microtubule-associated protein 2, MRI = magnetic resonance imaging, NeuN = neuronal nuclear antigen, NF = neurofilament, NSE = neuron-specific enolase, Olig-2 = oligodendrocyte transcription factor-2, PNET = primitive neuroectodermal tumor, T1WI = T1-weighted imaging, T2WI = T2-weighted imaging, TP = tumor protein, WHO = World Health Organization.

Keywords: cerebellar liponeurocytoma, computed tomography, immunohistochemistry intracerebral, magnetic resonance imaging

1. Introduction

Cerebellar liponeurocytoma is a rare tumor of the central nervous system (CNS), and was first introduced by Bechtel et al[1] in 1978 as a mixed mesenchymal and neuroectodermal tumor of the cerebellum. Previously, the neoplasm had been reported under variable names such as lipidized medulloblastoma, lipomatous medulloblastoma, and neurolipocytoma.[2–5] In the 2000 World

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Ethical Experimentation: This study was approved by the Ethical Committee of Beijing Tiantan Hospital, Capital Medical University (acquired SIDCER/FERCAP certification). All procedures performed in this study involving the patient were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

The authors have no conflicts of interest to disclose.

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Health Organization (WHO) classification of tumors of the CNS, cerebellar liponeurocytoma was recognized as a distinct clinicopathological entity under the heading of glioneuronal tumor and was defined as WHO grade I. However, the tumor was revised to grade II in the 2007 WHO classification owing to its low proliferation but high likelihood of recurrence, and the definition is still in use in the 2016 WHO classification.[6–8]

Cerebellar liponeurocytoma is predominantly located in the cerebellar hemisphere and vermis, and occasionally in the supratentorial lateral ventricle. There have been approximately 47 reported cases of cerebellar and 14 cases of intraventricular liponeurocytoma in the English literature.[9–13] However, so far, there have been no cases of supratentorial intracerebral liponeurocytoma reported in the literature. The tumor exhibits typically morphological characteristics including neurocytic neoplastic cells expressing both neuronal and glial markers and focal lipomatous differentiation. Although clinical manifestations, radiological findings, and histopathological features have been reported in the literature, the biological behaviors of the tumor and clinical prognosis of affected patients are still poorly understood, especially for supratentorial intracerebral liponeurocytoma. Recently, some reports indicated that patients with cerebellar liponeurocytoma usually present a favorable clinical course after surgical removal, but it needs to be emphasized that a long-term follow-up should be considered because of a higher likelihood of recurrence many years after initial resection.

Herein, we report the first case of cerebeller liponeurocytoma originating in the supratentorial cerebral hemisphere in a pediatric patient, and discuss the clinical, radiological, histopathological, therapeutic, and prognostic features of supratentorial intracerebral liponeurocytoma.

2. Methods

2.1. Patient information

This study was preapproved by the Beijing Tiantan Hospital Institutional Review Boards. We reviewed our records at the Department of Radiology and Neuropathology, Beijing Tiantan Hospital, Beijing Neurosurgical Institute, Capital Medical University, over a period of 16 years from July 2000 to March 2017. Here, we focus on a single case of cerebellar liponeurocytoma originating in the supratentorial cerebral hemisphere. We reviewed the clinical and radiological data, and contacted the patient and his family members to obtain his serial follow-up data.

2.2. Histopathological examination

The removed tumor tissue was routinely processed. Tissue sections were stained with hematoxylin and eosin (H&E); immunohistochemical analysis was also conducted using the indirect immunoperoxidase technique with antibodies to glial fibrillary acid protein (GFAP) (1:50; BioGenex), neuron-specific enolase (NSE) (1:100; Dako), synaptophysin (1:50; Dako), microtubule-associated protein 2 (MAP-2) (1:1000; Sternberger Monoclonals), neuronal nuclear antigen (NeuN) (1:50; BioGenex), S-100 (1:100; BioGenex), neurofilament (NF) (1:1000; BioGenex), oligodendrocyte transcription factor-2 (Olig-2) (1:50; BioGenex), and MIB-1 (1:50; Dako).

3. Results

A previously healthy, 11-year-old boy was admitted to the Ordos Center Hospital in Inner Mongolia, China owing to a progressive headache. A computed tomography (CT) scan showed an irregular hypodense and isodense mixed mass in the right frontal lobe. The diameter of the mass was approximately 4.5 cm. Twenty days later, he was transferred to our institution for further treatment.

In our hospital, the boy complained of an intermittent headache with nausea and vomiting in the morning; there were no seizures or disorder of consciousness. Magnetic resonance imaging (MRI) revealed a large cystic—solid mass approximately $4.5 \times 4.7 \times 6.4$ cm in size, in the right frontal lobe. The solid part of the mass exhibited heterogeneous isointensity on T1-weighted imaging (T1WI) and T2-weighted imaging (T2WI). Several spots of hypointensity in the solid part of the lesion were observed on T1WI and T2WI, and a few patches of slight hyperintensity on T1WI and hypointensity on T2WI were also found. The cystic part of the lesion was observed with uniform hypointensity on T1WI and hyperintensity on T2WI. The solid part and cystic wall were clearly enhanced after gadolinium administration (Fig. 1A–C). Moderate perilesional edema was also observed. The anterior horn of the right lateral ventricle was compressed, and the brain midline was shifted to the left.

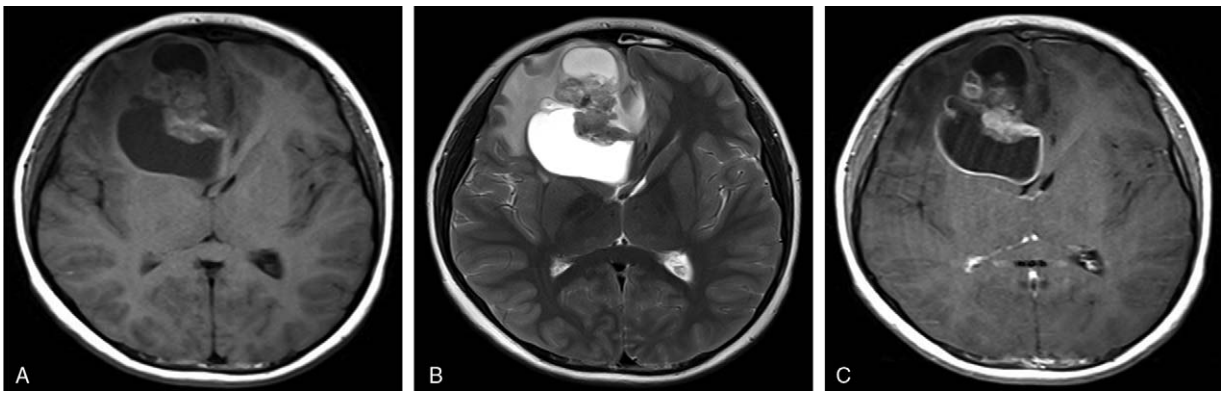

Figure 1. MRI findings. MRI shows an irregular, cystic—solid mass approximately $4.5 \times 4.7 \times 6.4$ cm in size, with surrounding edema in the right frontal lobe. The solid part and cystic wall of the lesion exhibit isointensity on (A) T1WI and (B) T2WI. Several spots of hypointensity on T1 and T2WI, as well as patches of slight hyperintensity on T1WI are also shown in the solid part of the tumor. (C) Contrast enhancement is clearly observed in the solid part and cystic wall. T1WI, T1-weighted image; T2WI: T2-weighted image. MRI = magnetic resonance imaging, T1WI = T1-weighted imaging, T2WI = T2-weighted imaging.

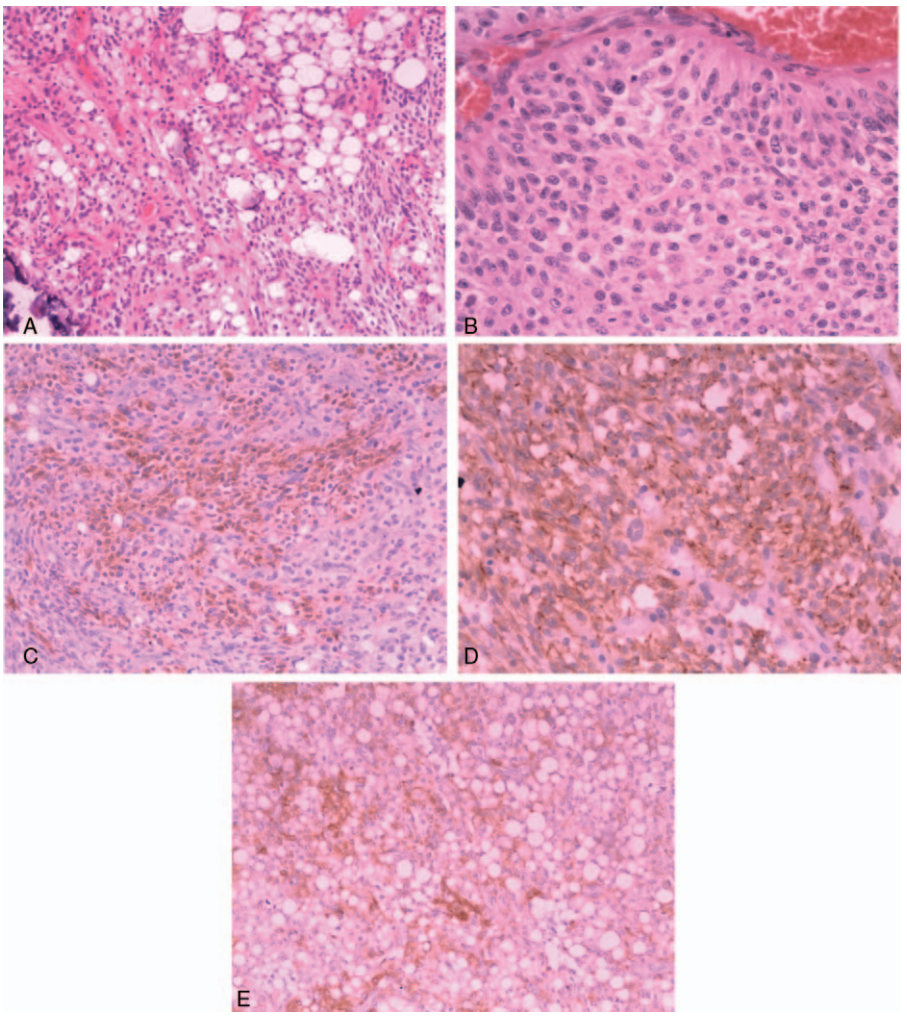

Figure 2. (A, B) Histopathological and (C–E) immunohistochemical features. (A) H&E stained section shows sheets of relatively isomorphic tumor cells with round nuclei, clear cytoplasm, and large lipid vacuoles among neoplastic cells (original magnification ×200). (B) Tumor cells have round nuclei with indistinct nucleoli and fine chromatin (original magnification ×400). (C) Tumor cells are diffusely immunoreactive for synaptophysin. (D) Tumor cells show strong labeling with MAP-2. (E) NeuN is focally positive in tumor cells (original magnification ×200). H&E = hematoxylin and eosin, MAP-2 = microtubule-associated protein 2, NeuN = neuronal nuclei antigen.

The lesion was surgically removed through a right fronto-parietal craniotomy. Under operative microscopy, the mass was mostly located on the surface of the right frontal lobe, and involved in the anterior cranial fossa and lateral sulcus cistern. The tumor was gray-white, cystic—solid, and filled with yellowish fluid. Gross total resection of the tumor was achieved. Adjuvant radiation therapy was not administered in the postoperative period. No clinical or neuroradiological evidence of recurrence or residual of the tumor was found 6 years and 2 months after initial surgery.

Histopathological examination showed a grayish appearance with lipoid tissue on the sections of the gross specimen. The H&E stain revealed isomorphic, small, round neoplastic cells resembling neurocytes and focal lipomatous differentiation. The tumor cells showed round nuclei, clear cytoplasm, and close arrangement (Fig. 2A and B). In immunohistochemical analysis, synaptophysin (Fig. 2C) and MAP-2 (Fig. 2D) immunopositivity were detected, and NeuN (Fig. 2E) and GFAP were also focally observed. Tumor cells were negative for Olig-2. MIB-1 antibody immunolabeling was detected in approximately 1.5%.

4. Discussion

Cerebellar liponeurocytoma is a very rare tumor with distinctive morphologic features of the CNS that arises in adults. This tumor is mainly involved in the cerebellar hemisphere and vermis, and occasionally involved in the lateral ventricle. The peak incidence is from 30- to 60-year-old, and the mean age of incidence is approximately 53 years. Men and women are affected equally. In this present case, the patient was an 11-year-old boy; the age of onset was evidently less than the mean age reported in the literature. The tumor originated in the right frontal lobe with invasion of the corpus callosum. Supratentorial intracerebral liponeurocytoma has not been reported in the literature previously. The main clinical manifestations of this patient were headache, nausea, and vomiting. These symptoms may be related to increased intracranial pressure resulting from mass effect and hydrocephalus.

Cerebellar liponeurocytoma usually appears as a solid mass on CT and MRI scans, and microcysts may occasionally be observed in the tumor. The focal areas of marked hypodensity on CT scans and hyperintensity on T1WI corresponding to fatty tissue inside

the tumor are characteristic findings, and the features may help preoperatively determine an accurate diagnosis of cerebellar liponeurocytoma.[10] The tumor in the present case was situated in the right frontal lobe, and appeared to be cystic—solid with mixed signal changes, as well as nodular enhancement in the solid component and ring-like contrast in the cystic wall with moderate peritumoral edema. These features were very different from those revealed in published case reports of cerebellar and intraventricular liponeurocytomas. The isointensity on T1WI and T2WI revealed the neoplastic cells intensively arrayed in the solid part of the tumor. The several spots of hypointensity scattered over the solid part might indicate areas of calcification, and the patches of slight hyperintensity, perhaps suggested the presence of some hemorrhage. The heavy contrast in the solid part and non-enhanced cystic components of this tumor implied disproportional vascularity and necrotic changes due to absent blood supply. The hyperintensity on T1WI reflecting fatty tissue was not observed because of lower fat content inside the tumor.

Regarding histopathological characteristics, cerebellar liponeurocytoma is composed of sheets of isomorphic round tumor cells and focal lipomatous differentiation. The neurocytic tumor cells possess round to oval nuclei enclosed within clear cytoplasm, and focal lipomatous change presented in clusters or scattered among small tumor cells.[14–16] Immunohistochemical staining reveals both neuronal and glial differentiation: for example, positive for synaptophysin, NSE, and MAP-2, and focal expression of GFAP. The MIB-1 labeling index is typically between 1% and 3%, but may increase to 5.8% in recurrent tumors.[10,17,18] The tumor in this study showed the histopathological features of cerebellar liponeurocytoma, such as isomorphic small neurocytic cells, round nuclei, clear cytoplasm, and focal lipomatous differentiation. More importantly, the tumor cells diffusely expressed synaptophysin and MAP-2, and exhibited focal positivity for NeuN and GFAP. Based on these histopathological findings, cerebellar liponeurocytoma originating in the supratentorial cerebral hemisphere was diagnosed. Microcysts may sometimes be observed in intraventricular liponeurocytoma, but large cystic degeneration inside this tumor was very rare.

Lipomatous variants of more typical tumors of the CNS are well known, including lipomatous medulloblastoma, cerebellar astrocytoma, oligodendroglioma, pleomorphic xanthoastrocytoma, and central neurocytoma, and occasionally in glioblastoma, ependymoma, and supratentorial primitive neuroectodermal tumor (PNET). As for this patient, the main differential diagnosis included oligodendroglioma and extraventricular neurocytoma; however, oligodendroglioma lacks immunohistochemical expression of neuronal markers such as synaptophysin and MAP-2.[14] With genetic analysis, 50–80% of oligodendrogliomas are known to harbor a chromosome 1p/19q co-deletion and a high frequency of *RI32H IDHI* mutations, while liponeurocytoma is considered to harbor a lack of 1p/19q deletions.[19,20] Cerebellar liponeurocytoma usually reveals a tumor protein (TP) 53 missense mutation with a higher frequency than that in medulloblastoma and lack of isochromosome 17q, a genetic hallmark of cerebellar medulloblastoma.[16,21] Extraventricular neurocytoma occasionally shows lipomatous differentiation inside the tumor, but complementary DNA (cDNA) expression suggests that TP 53 mutations are absent in central neurocytomas, indicating that their genetic pathways are different between central neurocytoma and intracerebral liponeurocytoma.[9]

Whenever feasible, total surgical resection is considered the standard treatment for cerebellar liponeurocytoma. Radiation therapy may still play a role in local recurrence treatment following incomplete excision or in tumors with a high proliferation index such as MIB-1. Some related reports have indicated that the recurrence rate in cerebellar liponeurocytoma is 31%,[22] but as it occurs following long disease-free intervals, repeat surgical removal may be preferable to radiotherapy. At present, there is still no agreement on postoperative adjuvant therapy because of the lack of clinical cases and long-term follow-up data.

Cerebellar liponeurocytoma usually has a benign clinical course, but local recurrence may appear a long time after incomplete resection. Prognostic evaluation of the tumor is very difficult. Kleihues et al suggested that the 5-year survival rate of cerebellar liponeurocytoma is 48%, but this should be interpreted with caution because of its rarity and the paucity of systematic follow-up data.[6,10] In this present case, the tumor originated in the supratentorial cerebral hemisphere and was defined as WHO grade II. The pediatric patient underwent gross total resection of the tumor, and was not treated with adjuvant therapy. No neurological evidence and radiological findings of recurrence or residual of the tumor was observed 6 years and 2 months after initial surgery at outpatient serial follow-ups.

5. Conclusions

Cerebellar liponeurocytoma is a rare tumor of the CNS. Herein, we have described the first case of cerebellar liponeurocytoma originating in the supratentorial cerebral hemisphere. This report suggests that intracerebral liponeurocytoma shows the same histopathological and immunohistochemical characteristics as liponeurocytomas located in the cerebellum and lateral ventricle. We propose a change in nomenclature of these tumors to use "central liponeurocytoma" instead of "cerebellar liponeurocytoma" to encompass all putative sites in future WHO classifications. Further studies based on long-term follow-up are necessary to determine biological behaviors, clinical features, and exact prognoses.

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