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Case Report

Cerebellar liponeurocytoma in the posterior fossa: a case report and review of the literature

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Abstract: Liponeurocytoma occurs primarily in the cerebellum, but a few cases have been documented to occur outside the cerebellum such as the lateral ventricle. However, liponeurocytoma is rarely observed at the bottom of the posterior fossa, and one case is reported in this study. The patient was a 54-year-old female who experienced headache for one year. MRI suggested that the root of the lesion was attached to the dura mater at the bottom of the posterior fossa. The base of the tumor was wide, and the boundary of the lesion with the cerebellum was clear. Flair imaging showed slight hyper signals within the lesion. The size of the tumor was approximately 2.5 cm, the lesion exhibited a regular pattern, and the edge was clear. During the surgery, the tumor was completely resected. The pathological examination and immunohistochemical diagnostic indicated cerebellar liponeurocytoma. Radiotherapy and chemotherapy were not implemented after surgery, whereas follow-up was performed for two years after surgery. The patient could manage her life independently, and her condition was excellent. Except learning the case in the paper, other cases of cerebellar liponeurocytoma were reported to occur outside the cerebellum. Different opinions on current treatment regimens were also reviewed in order to increase our understanding of cases of liponeurocytoma that occur outside the cerebellum, to avoid missed diagnoses and misdiagnoses, and to obtain the best treatment and prognosis.

Keywords: Central nervous system, liponeurocytoma, cerebellum

Introduction

Liponeurocytoma is a kind of rare neuroectodermal tumor that occurs in the central nervous system (primarily in the cerebellum) and that is characterized by growing slowly [1-3]. Historically, this tumor has ever had many names such as lipomatous medulloblastoma, lipidized medulloblastoma, neurolipocytoma, lipomatous glioneurocytoma, and lipidized mature neuroectodermal tumor of the cerebellum [4, 5]. This tumor type was termed as cerebellar liponeurocytoma in the pathology and genetics section of the 2007 World Health Organization (WHO) Classification of Tumors of the Central Nervous System; this tumor type was categorized as a mixed neuronal-glial tumor and was classified as WHO grade II [6]. Since the first case reported in 1978 [7], more than 40 cases have been reported in the literature [8]; however, only more than 10 cases have been reported to occur outside the cerebellum. This study reported a single case of cerebellar liponeurocytoma that occurred at the bottom of the posterior fossa with successful management by surgery without chemotherapy and radiation treatment. The occurrence of liponeurocytoma at this location is very rare. As one of the differential diagnoses of the central nervous system tumors, this case deserved serious consideration.

Case report

The patient in this case was a 54-year-old female who sought treatment at the First Hospital of Jilin University on December 9th, 2013 due to persistent headache for more than one year and worsening of the headache for one month. The patient complained of headache in November 2012, because this symptom was mild, the patient did not receive systemic treatment. Nearly a month ago, the patient perceived significant aggravation of the

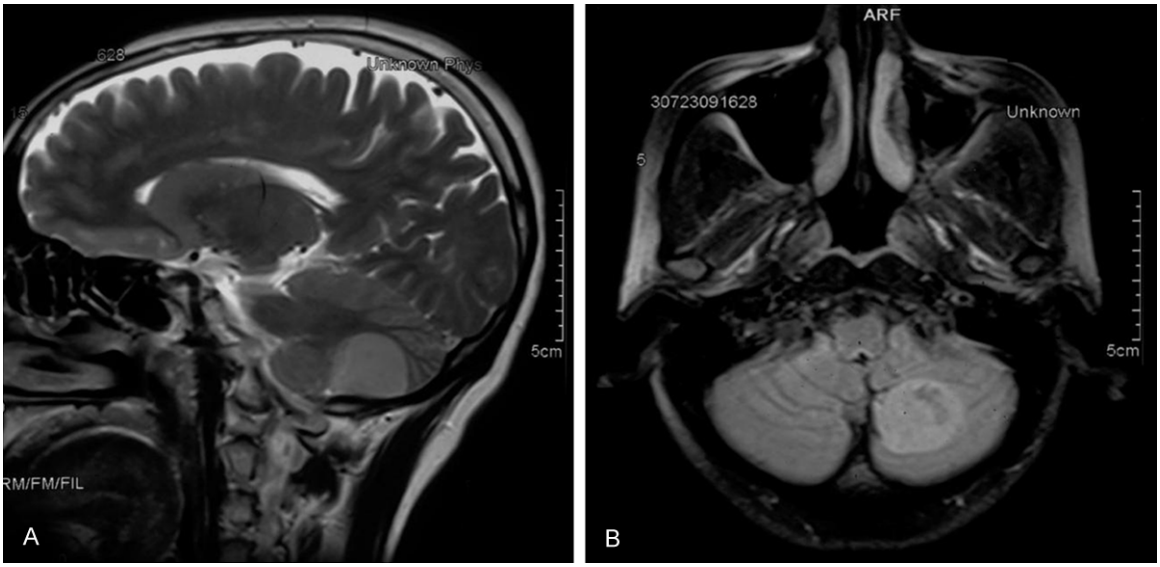

Figure 1. Cranial MRI images: A. T2WI showed that the root of the lesion was attached to the dura mater at the bottom of the posterior fossa. The base of the tumor was wide, and the boundary of the lesion with the cerebellum was clear. B. The axial Flair images showed slight hyper signals within the lesion. The size of the tumor was approximately 2.5 cm, the edge was clear.

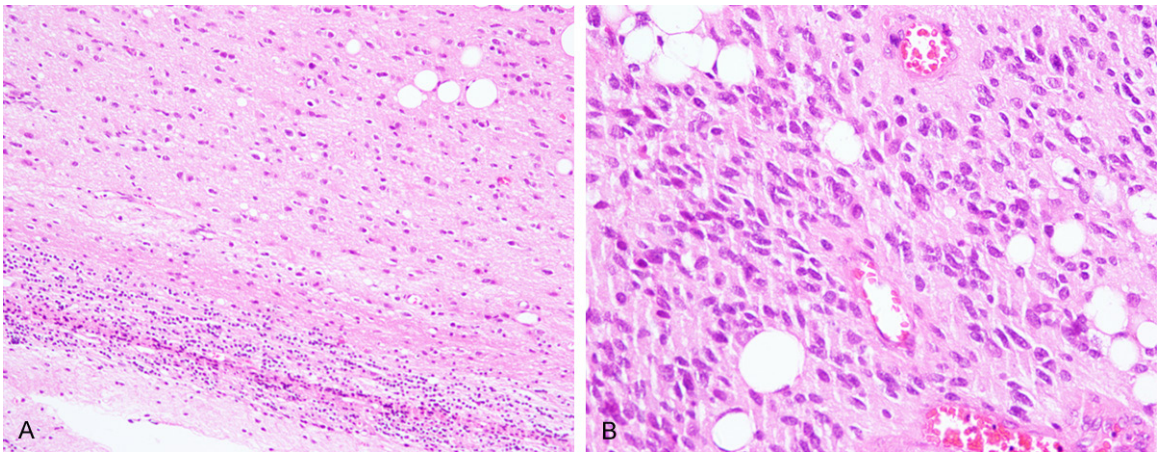

Figure 2. Histology of cerebellar liponeurocytoma: A. The edge of the tumor tissue contained normal cerebellar cells (Hematoxylin and Eosin (H&E), × 200). B. The tumor cells were arranged in the tight manner, and the majority of cells displayed neuronal morphology. The aggregation of multifocal adipocytes was also observed. (H&E), × 400.

headache with intermittent dizziness. The patient was then treated at the Tumor Hospital of Jilin Province in November 2013. The cranial MRI examination suggested the following: the lesion was attached to the dura mater at the bottom of the posterior fossa, the base of the tumor was wide, and the boundary of the lesion with the cerebellum was clear. Flair imaging showed slight hyper signals. The tumor size was approximately 2.5 cm, the edge of the tumor was clear, and the homogeneous enhancement was observed after contrast-enhancement (**Figure 1**). Throughout the disease course, the patient had an excellent diet, normal sleep patterns, normal defecation and micturition, and no reduction in body weight. The physical examination, which was performed after the patient was admitted, demonstrated that the patient had normal cognition and language, both pupils were round, had a diameter of 3.0 mm, and were sensitive to light reflection. The limb function was excellent, and muscle strength and

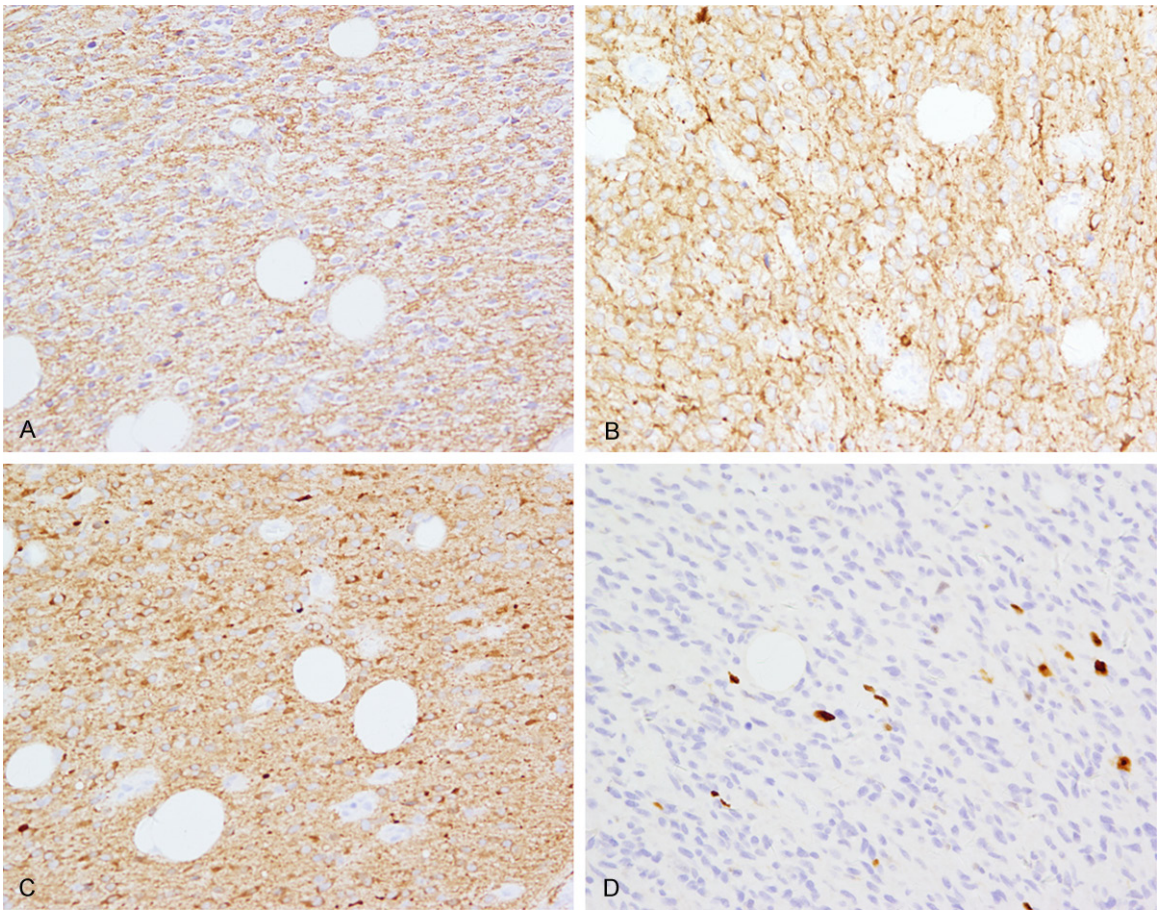

Figure 3. Immunohistochemical staining of cerebellar liponeurocytoma according to the two-step EnVision method (× 400). A. IHC for GFAP revealed diffuse positive expression in the tumor cells. B. MAP-2 staining showed diffuse positive expression in the tumor cells. C. NSE staining also showed diffuse positive expression in the tumor cells. D. The tumor cells had a very low Ki67 labeling index (< 5%).

tension were normal. The patient had a positive left hand finger test, a positive bilateral heel-knee-tibia test, a positive Romberg sign, and a negative bilateral pathology sign. The surgery was performed via a straight posterior median incision. After the dura mater was opened, the tumor was observed at the bottom of the posterior fossa. The tumor was light yellow in color, the texture was firm and tough, a complete capsule was present, and the blood supply was abundant. The base of the tumor rested on the dura mater at the bottom of the posterior fossa, and the boundary between the tumor and the normal brain tissue was clear. The tumor was completely resected and sent for pathological examination.

The pathological examination revealed a nodule-like mass, which was observed by the naked eye. The surface was gray-white or light brown in color, and the volume was approximately 3.5 cm × 2.5 cm × 2.0 cm. The tumor was also partially encapsulated. The section of tumor was solid and soft, light brown in color. The local area of the tumor was slightly semi-transparent. Under microscopy, the tumor cells appeared tightly arranged, the morphology was homogeneous, and the cells were medium in size. The nuclei of the tumor cells were round or oval in shape, the chromatin was slightly rough, the nucleoli were not obvious, mitotic figures were rare, and the different sized fibrous regions without nuclei were observed. In addition, scattered, flaky, and clustered fat-like cells were observed, which accounted for 20% of the total tumor components. The tumor tissues were surrounded by abundant blood vessels, and normal cerebellar tissues were observed at the edge (**Figure 2**). Immunohistochemistry showed that the tumor cells exhibited positive,

Table 1. Case material

Number	Sex/Age (yr)	Tumor location	Authors [Ref. No]
1	M/30	Left Lat v., 3rd v., CC	Horoupian, 1997 [10]
2	F/59	Anterior horn, Left Lat v.	George, 2001 [11]
3	M/30	Frontal horn, Lat v.	Rajesh, 2003 [12]
4	F/4	4th v.	Jouvet, 2005 [13]
5	M/35	Left Lat v.	Kuchelmeister, 2006 [14]
6	M/35	Lateral horn, Right Lat v.	Pankaj, 2010 [15]
7	F/45	Trigone of Lat. v.	Gupta, 2011 [16]
8	M/36	Bilateral Lat v.	Chakraborti, 2011 [17]
9	M/30	Lateral and 3rd v.	Chakraborti, 2011 [17]
10	M/32	Bilateral Lat v., central	Chakraborti, 2011 [17]
11	M/49	4th v.	Chung, 2012 [9]
12	M/34	3rd v.	Karabagli P, 2014 [8]
13	F/54	posterior fossa	Present case

Lat v. - lateral ventricle, 3rd v. - third ventricle, 4th v. - fourth ventricle.

diffuse expression of glial fibrillary acidic protein (GFAP) (**Figure 3A**), microtubule-associated protein (MAP-2) (**Figure 3B**) and neuron-specific enolase (NSE) (**Figure 3C**). In contrast, the tumor cells exhibited weak positive expression of neuron-specific nuclear protein (NeuN) and synaptophysin (Syn) and had a Ki67 index of < 5% (**Figure 3D**). The pathological diagnosis was cerebellar liponeurocytoma, which was classified as WHO grade II.

Radiotherapy and chemotherapy were not implemented after surgery, but follow-up was performed for 2 years after surgery. The patient was able to manage her life as usual, and her status was excellent.

Discussion

Liponeurocytoma is a kind of rare central nervous system tumor that occurs in the cerebellum. This tumor has benign histological characteristics and good clinical prognosis. The most common tumor location is the cerebellar hemisphere secondly the cerebellar vermis [8, 9]. Of course, these conclusions are based on information from more than 40 cases in the literature. However, in recent years, more than 10 cases of "cerebellar" liponeurocytoma that have occurred outside the cerebellum have been reported (**Table 1**). The most common location outside the cerebellum is the lateral ventricle. Additionally, this tumor type rarely occurs in the corpus callosum. In this case, the base of the tumor was located on the dura mater at the bottom of the posterior fossa, which has not yet been reported. This tumor appeared to have a pedicle, and the capsule was complete. Moreover, the tumor displayed nodule-like growth, and arachnoid interface was observed between the tumor and the brain stem. Moreover, the boundary of the tumor with the normal brain tissue was clear, and cerebellar tissue components could be observed under microscopy.

For any tumor, when the lesions occur in uncommon locations, some confusion in the diagnosis may arise, which complicates the differential diagnosis. The same phenomenon is seen in cases of liponeurocytoma when occurs outside the cerebellum. Only imaging diagnosis is not reliable because the presentation of cerebellar liponeurocytoma on imaging is very similar with adult ependymocytoma and medulloblastoma, especially medulloblastoma included lipid components. MRI T1 images of cerebellar liponeurocytoma revealed hypo-signals with scattered focal hyper signals, while T2 images of tumors showed moderate hyper signals with a mixed shape. Furthermore, the clinical presentation of liponeurocytoma is similar to that of the two types of tumors mentioned above; therefore, a diagnosis based on imaging alone is uncertain [18]. Once the tumor is discovered by imaging examination, surgical resection for pathological examination is necessary and accurate route in order to reach an acurrate diagnosis under the conditions permitted by these clinical indications. In this study, the cranial MRI examination of the patient suggested that the root of the lesion was attached to the dura mater at the bottom of the posterior fossa. The shape of the lesion was regular and the boundary was clear, which meant that the tumor conformed to the criteria for surgery. The tumor was completely resected and sent for pathological analysis.

According to the pathology and genetics section of the 2007 WHO Classification of Tumors in the Central Nervous System, this tumor was classified as cerebellar liponeurocytoma, WHO

grade II. However, we still need to carefully evaluate the histological changes that present in this tumor, because which can guide treatment methods and assess the prognosis from the results of recently observed cases. Some scholars have considered that the majority of cerebellar liponeurocytomas have a low proliferation index and better prognosis, patients have normal lives without radiotherapy and chemotherapy after total resection of the tumors. However, this does not exclude misunderstandings caused by the low incidence rate of this tumor and the lack of long-term systematic follow-up. Some statistical data showed that the recurrence rate reached 50% in patients who did not receive radiotherapy after their tumors were completely resected [5]. Buccoliero [1] reported a single recurrent case and reviewed the relevant literature. They speculated that when mitotic figures are present in liponeurocytoma and MIB-1-positive cells account for more than 10% of tumor cells, it should be considered a neoplastic lesion with uncertain malignant potential. Chatillon [5] considered that if the tumor cannot be completely resected or if it is totally resected but the tumor cell proliferation index is > 6%, radiotherapy should be considered. However, they also showed that radiotherapy could not prevent recurrence. The tumor cell proliferation index in this study was < 5%, and therefore, radiotherapy and chemotherapy were not implemented after surgery. After 2 years of follow-up, the patient's health status was normal.

Currently, unified standards in regards to the treatment methods for cerebellar liponeurocytoma are still uncertain. In addition, the evidence has not yet demonstrated whether the implementation of chemotherapy, radiotherapy, or radio-chemotherapy can prevent recurrence. Some authors have considered that the cell proliferation index of recurrent tumors is not significantly different than that of primary tumors. Moreover, slow growth and longer recurrence time are characteristics of these tumors; therefore, some have considered that radiotherapy might result in damage to nerve function and that radiotherapy after total tumor resection is not necessary. When the tumors recur, surgical treatment and adjuvant radiotherapy may be performed again [19]. Currently, no report has been published on the efficacy of chemotherapeutic drugs [3, 5]. On the condition that the tumor is completely resected and the tumor cell proliferation index was < 5%, we do not advocate the implementation of radiochemotherapy. However, regular observation should still be conducted, and long-term follow-up is absolutely necessary. The estimation of the prognosis of this tumor still requires further observation and examination.

The histogenesis of this tumor is still not clear. Currently, this tumor is thought to be derived from the neuroectoderm. Under microscopy, tumor cells include two morphologic types: one is a neuronal-like morphology where the cells are in a tight arrangement with a round or oval shape; the other type is a well-differentiated morphology of fat-like cells focally aggregated. Neuronal-like tumor cells express neuronal markers such as Syn, NSE, and MAP-2 and exhibit local expression of GFAP [3]. Positive expression of GFAP supports the theory of neuroectodermal origin. However, whether fat-like cells in the tumor result from the transitional changes that are associated with the conversion of neuroepithelial cells into adipocytes, the gradual accumulation of lipid droplets in the cytoplasm of tumor cells, or the cell degeneration is still not clear. Mena [20] also found that the neuronal markers Syn, GFAP, and S-100 were not expressed in these fat-like cells. Therefore, the determination of the tissue origin and the pathogenic mechanism of this tumor still require additional investigation using clinical cases and molecular biology-based experiments.

Conclusion

Cerebellar liponeurocytoma is not restricted to the cerebellum. We suggest that it would be more appropriate to name this tumor as a liponeurocytoma of the central nervous system. Our current understanding of cerebellar liponeurocytoma is based on sporadic case reports, as the data from large-scale studies are still lacking. Therefore, accurate epidemiological information still needs to be obtained. The presence of recurrence cases confirmed that the classification of this tumor as WHO grade II is correct. The problem in terms of treatment methods is whether radiotherapy or chemotherapy measures should be adopted after surgical resection of these tumors. The follow-up time for the majority of cases was not

sufficient; therefore, we anticipate subsequent follow-up results.

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Disclosure of conflict of interest

None.

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