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# Cerebellar liponeurocytoma - molecular signature of a rare entity and the importance of an accurate diagnosis

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ABSTRACT

*Background:* Cerebellar liponeurocytoma is an extremely rare tumour entity of the central nervous system. It is histologically characterised by prominent neuronal/neurocytic differentiation with focal lipidisation and corresponding histologically to WHO grade II. It typically develops in adults, and usually shows a low proliferative potential. Recurrences have been reported in almost 50% of cases, and in some cases the recurrent tumour may display increased mitotic activity and proliferation index, vascular proliferations and necrosis. Thus pathological diagnosis of liponeurocytoma is challenging. This case presentation highlights the main clinical, radiographic and pathological features of a cerebellar liponeurocytoma.

*Case presentation:* A 59-year-old, right-handed woman presented at our department with a short history of persistent headache, vertigo and gait disturbances. Examination at presentation revealed that the patient was awake, alert and fully oriented. The cranial nerve status was normal. Uncertainties were noted in the bilateral finger-to-nose testing with bradydiadochokinesis on both sides. Strength was full and no pronator drift was observed. Sensation was intact. No signs of pyramidal tract dysfunction were detected. Her gait appeared insecure. The patient underwent surgical resection. Afterward no further disturbances could be detected.

*Conclusions:* To date > 40 cases of liponeurocytoma have been reported, including cases with supratentorial location. A review of the 5 published cases of recurrent cerebellar. Liponeurocytoma revealed that the median interval between the first and second relapse was rather short, indicating uncertain malignant potential. The most recent WHO classification of brain tumours (2016) classifies the cerebellar liponeurocytoma as a separate entity and assigns the tumour to WHO grade II. Medulloblastoma is the most important differential diagnosis commonly seen in children and young adults. In contrast, cerebellar liponeurocytoma is typically diagnosed in adults. The importance of accurate diagnosis should not be underestimated especially in the view of possible further therapeutic interventions and for the determination of the patient's prognosis.

## 1. Background

Cerebellar liponeurocytoma (cLNC) is a rare tumour entity of the central nervous system. It histologically characterised by prominent neuronal/neurocytic differentiation with focal lipidisation and corresponding to WHO grade II [1]. It typically develops in adults, and usually shows a low proliferative potential. Recurrences have been reported in almost 50% of cases, and in some cases the recurrent tumour may display an increased mitotic activity and proliferation index, vascular proliferations and necrosis [2]. To date < 50 cases of liponeurocytoma have been reported, including cases with supratentorial location [3]. A review of the 5 published cases of recurrent cLNC revealed that the median interval between the first and second relapse was rather short, indicating a possible malignant progression [2]. The stan-

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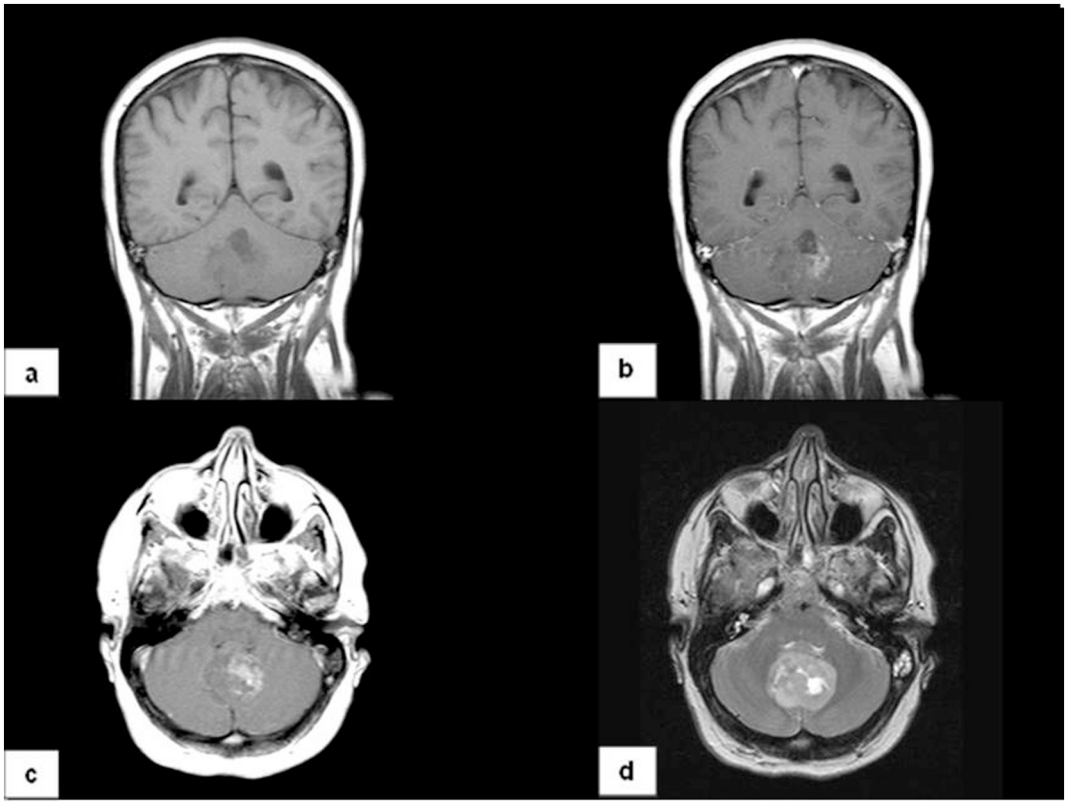


**Fig. 1.** The T1-weighted coronal sequence (a) shows an inhomogenously hypointense midline tumour of the posterior fossa. T1-hyperintense signal indicating fatty content was not detected. The lesion enhances gadolinium inhomogenously (b, c). Note the hyperintense signal of the tumour on T2-weighted sequence (d) and the regressively altered portions with almost fluid-equivalent T2 and T1 signal.

dard of care for treating cLNC is surgical resection followed by neuroimaging at regular intervals. Specific adjuvant therapies are not implemented.

## 2. Case presentation

### 2.1. History

A 59-year-old, right-handed woman presented at our department with a short history of persistent headache, vertigo and gait disturbances. Physical examination revealed that the patient was awake, alert and fully oriented. The cranial nerve status was normal. Uncertainties were noted in the bilateral finger-to-nose testing with bradydiadochokinesis on both sides. Strength was full and no pronator drift was observed. Sensation was intact. No signs of pyramidal tract dysfunction were detected. Her gait appeared unsteady. Magnetic resonance imaging (MRI) was obtained and confirmed a midline intraaxial tumour involving the inferior cerebellar vermis. The lesion was inhomogenously hypointense on the T1-weighted and hyperintense on the T2-weighted sequence with positive gadolinium (Gd) enhancement [Fig. 1a–d] and with minimal surrounding edema. Massive mass effect was evident by compressing the fourth ventricle with mild obstructive hydrocephalus.

### 2.2. Surgery and early post-operative MRI

The tumour was completely resected via a median suboccipital craniotomy. It was well-circumscribed, moderately vascularised and originated within the medial aspect of the inferior cerebellar vermis. The fourth ventricle did not have to be opened. The early postoperative MRI did not detect any tumour remnants [Fig. 2]. Cerebrospinal fluid pathways were restored.

The patient recovered well from the operation. Slight gait disturbances were noticeable. To this date, 3 years after the operation, serial neuroimaging did not detect a tumour relapse [Fig. 4a–d].

### 2.3. Histopathological and molecular data

Neuropathological examination revealed a prominent neuronal differentiation with focal accumulation of adipocytic cells [Fig. 3a and b]. The neurocytic areas expressed neuronal markers (e.g. synaptophysin), GFAP was focally positive [Fig. 3c and d] and Ki-67 was widely low (5%) [Fig. 3 inset].The routine molecular analyses showed a wild-type sequence for the IDH1 and IDH2 gene, a preserved ATRX nuclear expression, a negative 1p19q codeletion status and an unmethylated MGMT-promoter. Molecular classification by DNA Methylation Profiling was performed by the national competence center for gliomas for scientific reasons and to exclude a high grade glioma. The 450-K analysis revealed a high consensus score with the group of cerebellar liponeurocytoma and confirmed the diagnosis [Fig. 3e]. For this experimental analysis, the genome-wide DNA methylation profile is compared with > 1500 tumours of a tumour bank.

## 3. Discussion and conclusion

cLNC is a rare tumour entity of the central nervous system and typically diagnosed in adults. Medulloblastoma (MB) is the most important differential diagnosis often presented as an intraaxial tumour with close contact to the fourth ventricle. In contrast MB is commonly seen in children and young adults [4]. Histologically, MB has a more primitive or embryonal appearance than the neurocytic morphology observed in the cLNC [4]. Clear cell morphology and lipidised cells are

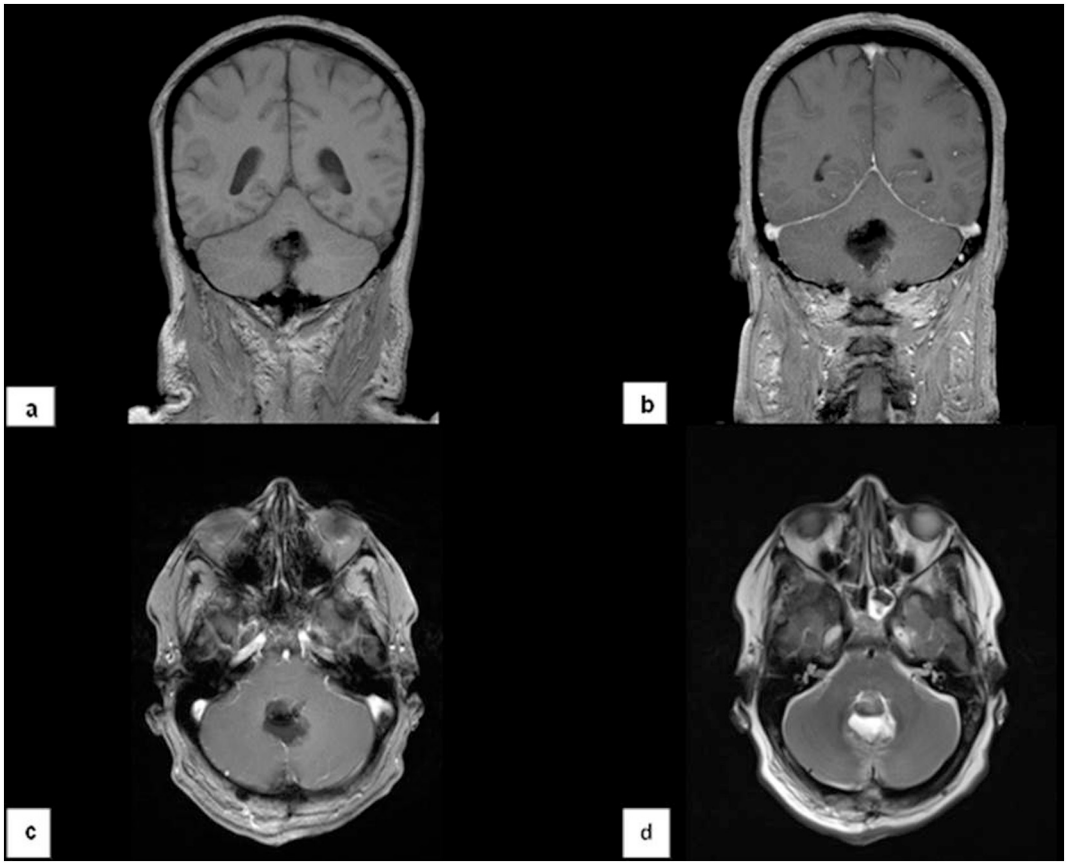


**Fig. 2.** The early postoperative MRI scan shows no evidence of enhancing or non-enhancing residual tumour. A midline resection defect with some air inclusions can be appreciated.

not typical findings in MB, but are seen in cLNC. “Generally the Ki-67 proliferation index for cLNC is significantly lower than that for MB and other high grade mimics, typically < 5%” [4,5]. Unlike astrocytic tumours, an IDH1 mutation is not commonly present in cLNC and there was no IDH1 mutation detected in the case presented here. A preserved ATRX nuclear expression and an unmethylated MGMT-promoter do not exclude a high grad glioma. But in combination with a widely low Ki 67 is not consistent with a high grade glioma. The negative 1p19q codeletion status excludes an oligodendroglioma.

The adipose tumour cells in MB may also show a typical clustering comparable to cLNC. However, a growth fraction of 15–40% is not consistent with newly diagnosed cLNC knowing the fact that proliferative indices of up to 20% were only found in very few primary and recurrent liponeurocytoma [4]. In addition, genetic analysis revealed cLNC as a distinct tumour entity without a relation to MB [1].

Central neurocytomas (cN) are typically located supratentorial in the lateral ventricles and/or in the third ventricle. Histologically they also correspond to WHO grade II. However, in contrast to these tumours, cLNC are mutated in TP53, indicating that their development is regulated by different signaling pathways [1].

The importance of an accurate diagnosis should not be underestimated, since misdiagnosis could lead to wrong decisions concerning further therapeutic strategies. There is no need for a change of the current diagnostic standards. But in case of doubt a reference diagnosis is of elementary importance. Molecular classification by DNA methylation-profiling may be helpful and accelerates the confirmation of the diagnosis considering the fact that more common differential diagnosis like oligodendrogliomas, clear cell ependymomas, or especially high-grade tumours like medulloblastomas need to be adjuvantly treated more aggressively.

## List of abbreviations

| | |
|---|---|
| ATRX | Alpha-thalassemia/mental retardation syndrome X-linked |
| cLNC | Cerebellar Liponeurocytoma |
| Gd | Gadolinium |
| GFAP | Glial fibrillary acidic protein |
| IDH 1 | Isocitrate dehydrogenase 1 |
| IDH 2 | Isocitrate dehydrogenase 2 |
| MRI | Magnetic resonance imaging |

## Ethics approval and consent to participate

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. Ethical approval was not obtained according to the guidelines of our institution concerning publishing case report, a sufficient anonymization preconditioned.

## Consent for publication

A copy of the written consent is available for review by the Editor-in-Chief of this journal.

## Availability of data and material

All data generated or analyzed during this study are included in this published article.

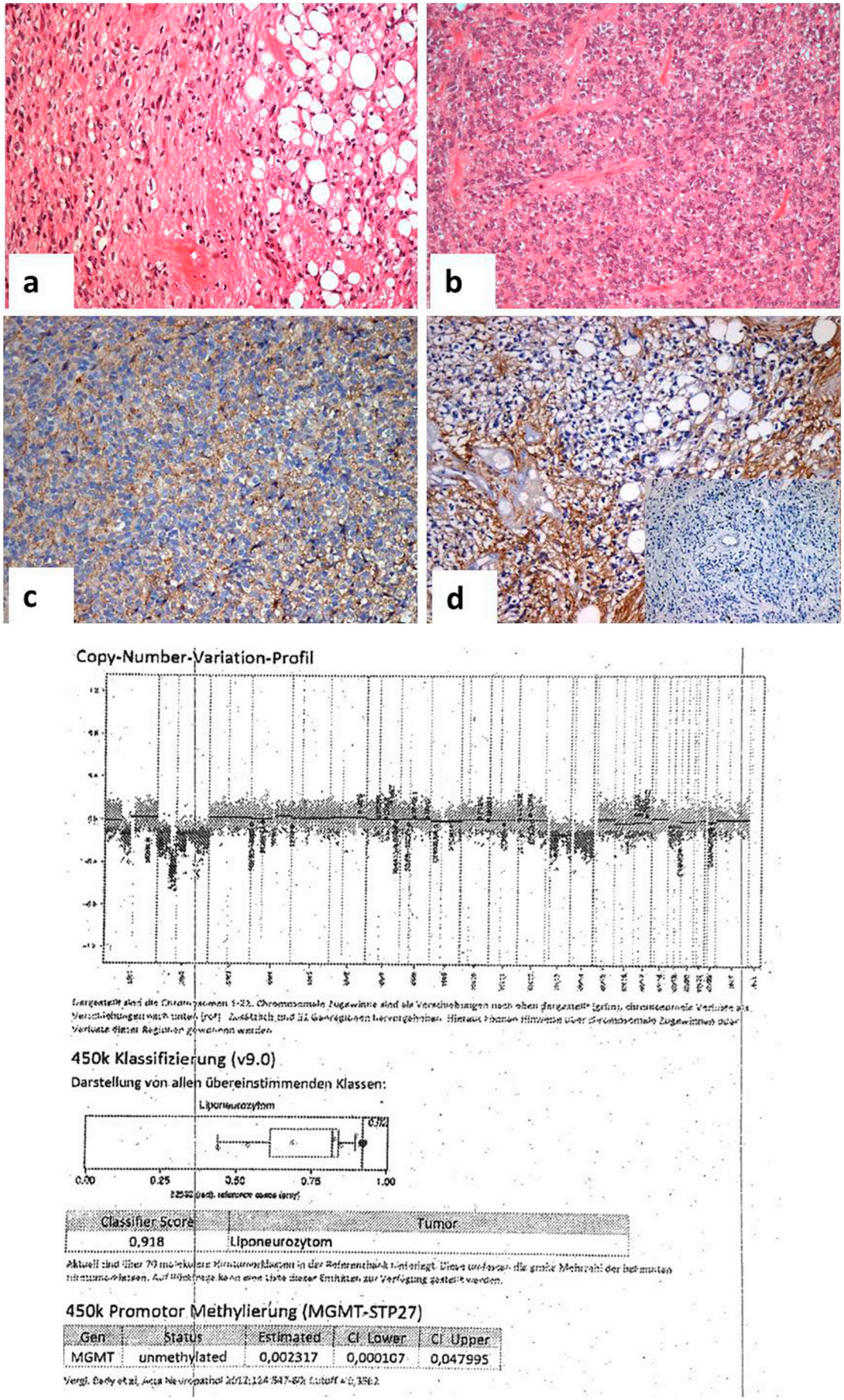


**Fig. 3.** a, b: Tumour sample of liponeurocytoma composed widely of a uniform population of small neurocytic cells with regular round to oval nuclei and focal accumulation of lipid-laden cells (H&E staining, 100×). Strong and diffuse expression of synaptophysin (c) and focal of GFAP (d), low Ki-67 proliferation index (inset). Molecular Classification by DNA Methylation Profiling DKFZ Heidelberg (e).

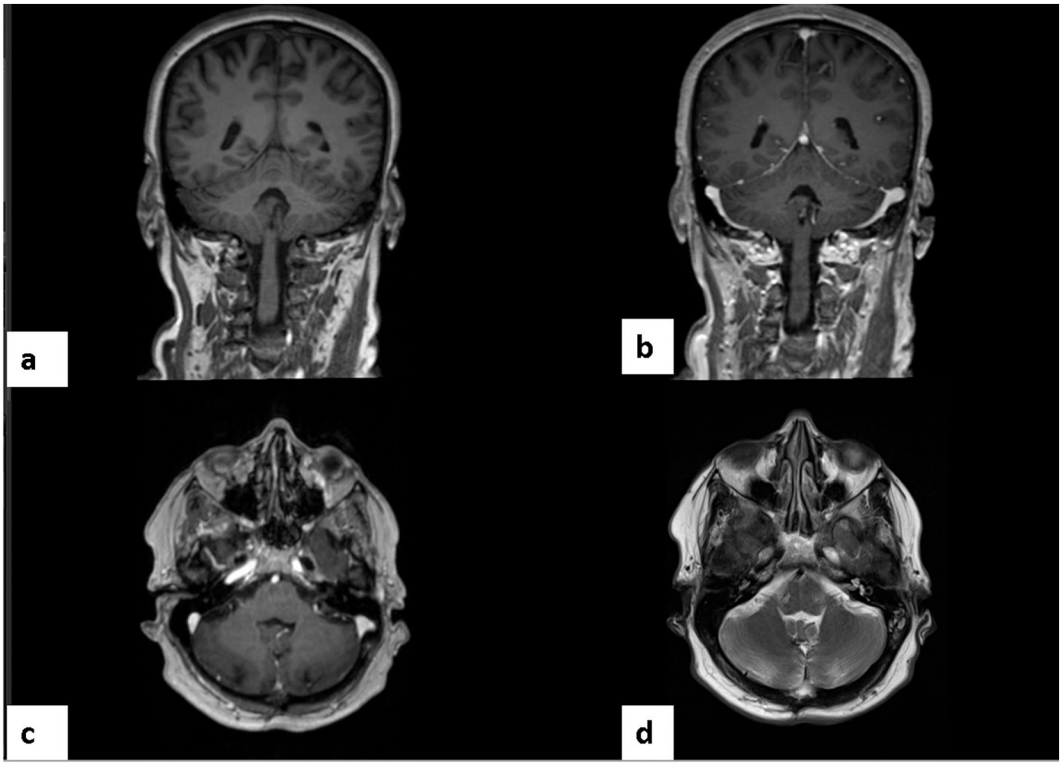


**Fig. 4.** MRI follow-up three years after resection. There are no evidences for tumour relapse.

## Competing interests

The authors declare that they have no competing interests.

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## CRediT authorship contribution statement

**Thomas Linsenmann:** Investigation, Writing - orginal draft, Conceptualization, Data curation. **Camelia M. Monoranu:** Investigation, Conceptualization, Data curation. **Balint Alkonyi:** Investigation, Conceptualization, Data curation. **Thomas Westermaier:** Writing - review & editing, Conceptualization, Data curation. **Carsten Hagemann:** Writing - review & editing, Conceptualization, Data curation. **Almuth F. Kessler:** Writing - review & editing, Conceptualization, Data curation. **Ralf-Ingo Ernestus:** Writing - review & editing, Conceptualization, Data curation. **Mario Löhr:** Writing - review & editing, Writing - orginal draft, Conceptualization, Data curation.

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