Case Report

Does “Cerebellar Liponeurocytoma” Always Reflect an Indolent Biological Behaviour?:
An Unusual Case With Review of The Literature
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Summary
A rare tumor, cerebellar liponeurocytoma is classified into glioneuronal tumors under the 2000 World Health Organization (WHO) classification of tumors of the central nervous system. The current 2007 WHO classification assigns grade II to the cerebellar liponeurocytoma. Tumors are predominantly localized in cerebellar hemispheres, and the second most common location is the vermis. In the report, an unusual case of cerebellar liponeurocytoma was presented with clinically and histologically aggressive features. In future tumor classification, it should be considered that its biologic behavior is not as indolent as suggested by current literature. This tumor should be regarded as an uncertain malignant potential lesion when mitoses are present and the MIB-1 positive cells are more than 10%.

Key words: Liponeurocytoma-cerebellar-aggressive-MIB-1-p53

INTRODUCTION
Cerebellar liponeurocytomas have been included in the 2000 World Health Organization (WHO) classification of tumors of the central nervous system, under heading of glioneuronal tumors. As a rare cerebellar neoplasm of adults this tumor is composed of neuronal, variable astrocytic and focal lipomatous differentiation, and showing a low proliferative potential. The current WHO classification therefore assigns the cerebellar neurocytoma to WHO grade...
In 1978, Bechtel et al. reported a case of lipomatous medulloblastoma in a 44-year-old man. The terms neurolipocytoma, medullocytoma, lipomatous glioneurocytoma, lipidized mature neuroectodermal tumor have also been proposed\(^\text{5,9}\). As a term, cerebellar liponeurocytoma is now largely accepted and is supported by genetic analyses that indicate that this lesion is not a variant of medulloblastoma\(^\text{6,9}\).

There have been approximately 40 reported cases. The mean age is 38.5 years (range 4-77 years), with male preponderance\(^\text{2,4,8,9,12}\). Tumors are predominantly located in cerebellar hemispheres, followed by a more central location in the vermis\(^\text{9}\). The tumor usually has a favorable clinical prognosis, although recurrences are frequent. However, the natural history and the long term prognosis for the tumor is being questioned, because of the rarity of this tumor\(^\text{4,7,11}\).

We report an unusual case of with divergent histological features. Characteristic features of these tumors are discussed in the light of pertinent literature.

**CASE PRESENTATION**

Reported is case of a 53-year-old woman with relapsing cerebellar liponeurocytoma which has occurred 3 times after the first radical excision of the primary lesion after 18 years. However, due to lack of obtaining the information for the former two surgical operations and their histopathological findings, there is comparable data to be used with the findings of present tumor. Three years ago she was undergone a third operation and was diagnosed as anaplastic ependymoma grade III. In her last admission her MRI scan showed a cystic, vascular, 6x5x5cm contrast enhancing mass in the right cerebellar hemisphere (Fig 1a-b).

The H&E stained paraffin sections showed a nodular tumor showing astrocytic cells which were supported a glial fibrillary matrix, uniform, round oligodendroglia-like cells containing round, “salt-pepper” nuclei and perinuclear halo, and focal lipidized cells (Fig 2a). The cells expressed NSE (Fig 2b), synaptophysin (Fig 2c), S-100, EMA, GFAP and vimentin. The p53 protein was detected in the majority of neoplastic cells and high proliferation activity, evaluated by MIB-1 antibody, was 33\% (Fig 2d). Histopathologic aggressive features like presence of atypia, mitoses (4/10HPF) and necrosis, endothelial proliferation were shown in last two recurrent tumor. Gross total resection and radiotherapy of the tumor was performed. At three year follow-up after fourth operation, MRI showed no tumor recurrence.

![](image)

**Fig 1a:** Sagittal. **1b:** Axial. On T1-weighted MRI scan showed a cystic, vascular, 6x5x5cm mass in right cerebellar hemisphere.
DISCUSSION

Liponeurocytomas are rare cerebellar neoplasm with benign histological features and a favorable clinical prognosis. However, current clinical opinion is based on a total of approximately 40 published cases\(^{(2,7,9,12)}\). The current WHO classification assigns the cerebellar liponeurocytoma to grade II, because recurrences have been reported in 62% of cases\(^{(9)}\). There have been a number of recurrences, with a mean time from diagnosis to first local recurrence presentation of 10.6 (range 10-12) years\(^{(12,13)}\). Despite being clinically progressive, recurrent liponeurocytomas did not show histological features of malignant progression\(^{(9)}\).

Liponeurocytomas are characterized by many lipidized cells found in clusters or scattered between small neoplastic cells. Immunohistochemical staining has demonstrated that both neuronal and glial differentiation. Histologically mitotic activity and proliferation rate are generally low in these lesions\(^{(9,12,13)}\). There have been only two reported cases with histopathologic aggressive features in the literature\(^{(1,4,8,14)}\).

Cerebellar liponeurocytoma has a relatively benign clinical course and a recurrence may appear after a long period of time with a histology only slightly more aggressive than that of the original tumor\(^{(8)}\).

Jenkinson reported an unusual case of cerebellar liponeurocytoma that presented a first recurrence 12 months after subtotal removal followed by external beam radiation therapy of the first lesion and, a second recurrence three months after a second surgical removal. Despite the absence of atypical histological features in both the primary and the relapsed tumors,
the aggressive case described by Jenkinson suggested that cerebellar liponeurocytoma may not be as benign as previously thought(7).

A review of published cases indicates that 2 cases with several relapses and histopathologic aggressive features such as atypia, mitoses, necrosis and/or a high proliferation index. Both glial and neuronal differentiation were shown in all of them, as in present case (Table 1)(1,4,8,14).

In Jouvet's case report, the recurrence was histologically identical to the original tumor in some areas but with fewer adipose-like cells, while others presented an endocrine architecture with oligodendroglia-like or monomorphic cells. Proliferation index was quite high (10-15%), and had a more likely habit of recurrence (15-30%)(8).

Gallina et al. reported the another recurred cerebellar liponeurocytoma showing clinical and histopathological aggressive features. Some differences were observed between primary lesion and its recurrence. Mitoses and MIB-1 positive cells were elevated from rare to 2-3 and from 15% to 20%. Ultrastructurally detectable synaptic vecicles were found in the recurrence, but absent in the primary tumor. Areas of micronecrosis, microhemorrhage and moderate vascular hyperplasia were observed in the relapse(1,4,14).

Our case which has occurred 3 times after the first radical excision of the primary lesion after 9, 15, and 18 years respectively. Histopathologic aggressive features like presence of mitoses, necrosis and endothelial proliferation were shown both in last two recurrent tumors. MIB-1 antibody was 33% in last surgery specimen. Therefore this findings was regarded to be reflecting its aggressiveness by multiple recurrences. Because of the rarity of the tumor, the natural history of cerebellar liponeurocytoma has not yet been defined and benign nature of the tumor is being questioned(3,4). Cerebellar liponeurocytomas may not be as benign as the current literature. Their typical low-grade cytological and histological features may hide their ominous clinical course(11).

Cluster analysis of the cDNA expression data of 1176 genes grouped cerebellar liponeurocytomas close to central neurocytomases, but distinctive from medulloblastoma. Furthermore, the cDNA expression array data suggest a relationship to central neurocytomases, but the presence of the TP53 mutations (20%), which are absent in central neurocytomases, suggest that their genetic pathways are different(4,6,9). The p53 protein was detected in our case.

The most important differential diagnosis is that of medulloblastoma with lipidized cells. In these lesions, the adipose tumour cells are usually more diffusely distributed. Lipidized medulloblastomas also occur in children. The frequency of p53 missense mutations is higher than in medulloblastomas(9).

Total resection is considered the optimal treatment. There is no consensus regarding the treatment of liponeurocytoma, specifically whether chemo- and/or radiotherapy is an indispensable part of the postoperative treatment regimen(3,4,7,9,12).
Table 1: The review of previously reported clinically and histopathologically aggressive liponeurocytomas including the present case.

<table>
<thead>
<tr>
<th>Authors, (Refs)</th>
<th>Sex /Age (yr)</th>
<th>Site</th>
<th>Treatment</th>
<th>Ki-67 %</th>
<th>Histology</th>
<th>Follow-up</th>
<th>Outcome</th>
</tr>
</thead>
<tbody>
<tr>
<td>Taddei(14), 2001</td>
<td>M/61</td>
<td>Rt.</td>
<td>TR</td>
<td>2-3</td>
<td>HWR, R, M,N,V</td>
<td>Rec. 3,5 yrs postop.</td>
<td>ANR 4 yrs</td>
</tr>
<tr>
<td>Buccoliero(1),2005</td>
<td></td>
<td>Cer.</td>
<td>TR+RT</td>
<td>15-20</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Gallina(4), 2009</td>
<td></td>
<td>Hem.</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Jouvet(8), 2005</td>
<td>F/4</td>
<td>4. ventr.</td>
<td>SR</td>
<td>10-15</td>
<td>M rare, R</td>
<td>Rec. 14 months postop.</td>
<td>NDA</td>
</tr>
<tr>
<td>(present case)</td>
<td></td>
<td>Ceramic</td>
<td>TR</td>
<td>15-30</td>
<td>M rare</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cer.</td>
<td>R, 1998</td>
<td>NDA</td>
<td>NDA</td>
<td>Reop. Rec. 3 yrs postop</td>
<td>Reop. Rec. 3 yrs postop</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Hem.</td>
<td>R, 2004</td>
<td>NDA</td>
<td>M,N,V</td>
<td>ANR 2,5 yrs</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>TR+RT,2007</td>
<td>33</td>
<td>M,N,V</td>
<td></td>
<td></td>
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</table>

CONCLUSION

Current clinical opinion is based on a total of 40 published cases. In this report an unusual case of cerebellar liponeurocytoma was presented with clinically and histologically aggressive features.

We suggest biological behavior of liponeurocytoma is not as indolent as the current literature suggests. Cerebellar liponeurocytomas may not be as benign as the current literature and typical low-grade cytological and histological features suggest. This tumor should be regarded as an uncertain malignant potential lesion when mitoses are present and the MIB-1 positive cells are more than 10%.

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