Liponeurocytoma: Systematic Review of a Rare Entity

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Key words
- Adjuvant radiotherapy
- Liponeurocytoma
- Recurrence
- Surgery
- Systematic review

Abbreviations and Acronyms
CT: Computed tomography
DWI: Diffusion-weighted imaging
FLAIR: Fluid-attenuated inversion recovery
FDG: [^{18}F]fluorodeoxyglucose
IDH1: Isocitrate dehydrogenase 1
MRI: Magnetic resonance imaging
PET: Positron emission tomography

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OBJECTIVE: **Liponeurocytoma is a rare benign tumor of the central nervous system, which develops mainly in adult patients within the posterior fossa. The World Health Organization has categorized this entity in its last classification of 2016 as a benign grade II tumor. Histopathologic characteristics contain neuronal and variable astrocytic differentiation with foci of lipomatous distinction. Only a few case reports and case series have been reported and the knowledge of this tumor is limited. General treatment guidelines do not exist. The aim of this study was to analyze the literature to create treatment guidelines.**

METHODS: **PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines were followed to search existing online databases between January 1, 1978 and May 15, 2018.**

RESULTS: **A systematic review of the literature found 73 patients (40 female, 33 male) with liponeurocytoma, in 59 of whom (80.8%) the disease occurred in the posterior fossa. The Ki-67/MIB-1 proliferation index was described in 58 patients, showing a mean value of 3.73% ± 4.01%. Follow-up was performed in 49 patients, with a median length of 52.02 ± 50.52 months, showing tumor recurrence in 14 patients (28.57%). Tumor recurrence was observed in only 1 patient (1/12, 8.33%) after adjuvant radiotherapy, whereas tumor recurrence was seen in 13/29 patients (44.83%) who did not receive adjuvant radiotherapy.**

CONCLUSIONS: **Liponeurocytomas are rare benign tumors, occurring mainly in the cerebellum. The therapy of choice is surgery. Postoperative radiotherapy seems to decrease the risk of tumor recurrence and should be offered to the patient.**

INTRODUCTION

Liponeurocytoma is a rare tumor mainly located in the posterior fossa. It typically affects adults and harbors a favorable clinical prognosis.[1] Liponeurocytoma was first described in 1978 by Bechtel et al.[2] as a mixed mesenchymal and neuroectodermal tumor. Some previous cases were reported as "unusual medulloblastomas in adults," "lipomatous medulloblastomas," "lipidized medulloblastomas," "neurolipocytomas," or "medullocytomas."

The World Health Organization recognized liponeurocytoma in the World Health Organization classification of 2000 as cerebellar liponeurocytoma, emphasizing its neurocytic differentiation, and classified it into the group of neuronal tumors.[1] In 2016, the tumor was categorized as a neuronal/neurocytic tumor and classified as grade II as a result of long-term follow-up studies showing a higher recurrence rate than originally expected.[3]

It is histologically characterized by lipidized cells found in clusters or scattered between small neoplastic cells. Immunohistochemical staining shows advanced neuronal/neurocytic differentiation with a low proliferation index.[3,4]

Although imaging, pathologic, and immunohistochemical characteristics have been reported, clinical and pathologic diagnosis of the liponeurocytoma remains challenging and disease progression of this tumor entity is still poorly understood.

Accurate differential diagnosis of this rare central nervous system tumor from other brain tumors such as medulloblastoma or oligodendroglioma is important to avoid unnecessary aggressive adjuvant therapies.

Our systematic review aims to present an overview about the diagnostic, histopathology, and therapy of this entity to provide a better understanding of this unusual tumor.

METHODS

Systematic Review of the Literature

A systematic search via PubMed, Medline, Medline in process, the Cochrane Collaboration Library, Scopus, and Google Scholar was performed for literature published between January 1, 1978 and May 15, 2018 independently by 2 authors. A systematic search was performed using

the keywords "liponeurocytoma,", "cerebral liponeurocytoma,", "cerebellar liponeurocytoma,", "unusual medulloblastomas in adults," "lipomatous medulloblastoma," "lipidized medulloblastoma," "neurolipocytoma," or "medullocytoma."

Inclusion criteria were articles published in English presenting the clinical course, neuropathologic features, and the treatment regime.

After the initial work was completed, the reference lists of included articles were reviewed to identify and include additional eligible articles. Furthermore, all included studies were meticulously cross-referenced to ensure that patients were not included in multiple articles. The systematic review was conducted following PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines.[5]

RESULTS

Systematic Review

The search resulted in 2400 articles, 2227 of which were excluded after analyzing the title and abstract. The full text of the remaining 173 articles was reviewed and 108 articles were then excluded. Therefore, 65 articles met the inclusion criteria, giving 73 cases of liponeurocytomas (Figure 1).[2,6-69]

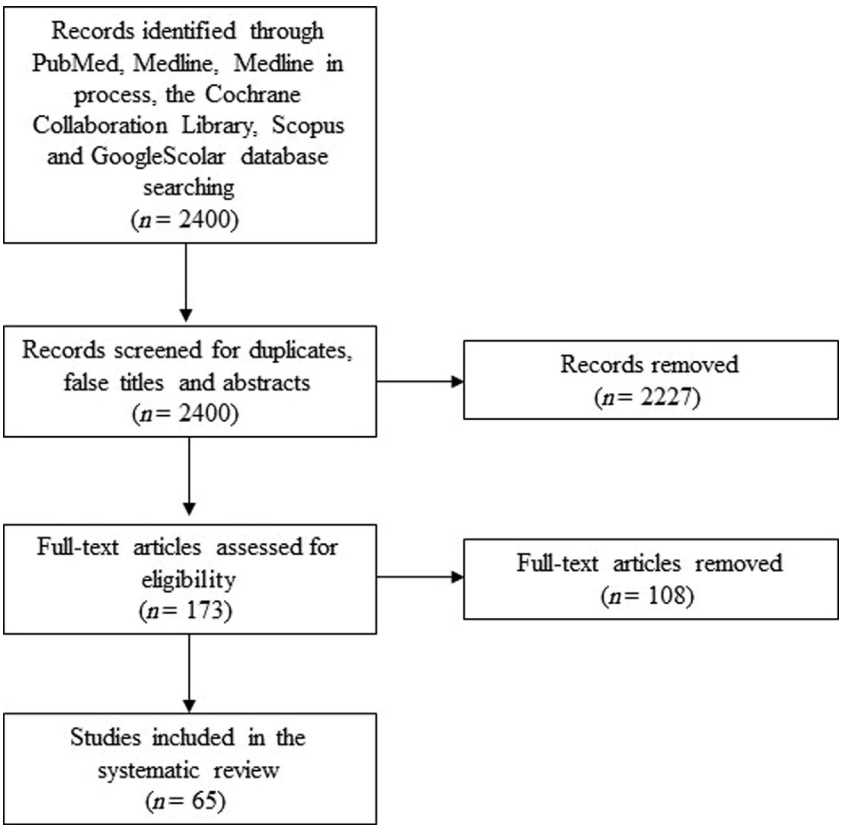

Figure 1. Flowchart showing systematic review of the literature.

Patients and Follow-Up

A systematic review identified 73 patients (40 female and 33 male) with a mean age of 45.26 ± 14.30 years (range, 4–77 years) (Table 1).

In 59 cases (80.8%), the tumor occurred in the posterior fossa, and in 14 cases (19.2%), the tumor was localized supratentorial next to or inside the ventricles.

Follow-up examinations were described in 50 patients with a median follow-up of 52.02 ± 50.52 months. Tumor recurrence occurred in 14 of 50 patients (28.0%) after 71.00 ± 50.98 months, whereas 36 patients (72.0%) remained tumor free over the same follow-up period. Second tumor recurrence was observed in 6 patients (42.86%) after 28.5 ± 21.61 months (Figure 2).

Histologic Parameters

The Ki-67/MIB-1 proliferation index was described in 55 cases, showing a mean value of 3.73% ± 4.01%. In addition, the Ki-67/MIB-1 proliferation index after first tumor recurrence was reported in 6 cases with a mean Ki-67/MIB-1 proliferation index of 9.16% ± 7.79%. The Ki-67/MIB-1 proliferation index after second recurrence was 20% in 1 reported case.

Histopathologically, the tumor showed positive immunoreactivity to synaptophysin (65/66 cases, 98.48%), neuron specific enolase (NSE) (27/27 cases, 100%), hexaribonucleotide binding protein-3 (NeuN) (16/16 cases, 100%), glial fibrillary acidic protein (GFAP) (53/62 cases, 85.48%), microtubule-associated protein 2 (MAP-2) (20/20 cases, 100%), S100-protein (23/28, 82.14%), and chromogranin A (6/11, 54.54%).

Neurofilament was negative in 21/31 cases (67.74%), tumor protein p53 (TP53) was measured in 9 cases, 5 of which were negative (Table 1).

Radiologic Characteristics

Liponeurocytoma was described as hypodense on computed tomography (CT) in 21/26 cases (80.77%) and as isodense in 4/26 cases (15.38%). One case was described as mixed intensity. Contrast enhancement, mostly irregular and heterogeneous, was detected in every case.

On magnetic resonance imaging (MRI), liponeurocytoma showed a hypointense characteristic on T1-weighted images in 22/40 reported cases (55%), isointensity was seen in 11/40 cases (27.5%), and only a few cases (7/40, 17.5%) were described as hyperintense on T1-weighted imaging. On T2-weighted images, hyperintensity was seen in 30/34 cases (88.25%) and isointensity was described in 3/34 cases (8.82%). In 1 case, hypointensity with hyperintense spots were described. On fluid-attenuated inversion recovery (FLAIR) imaging, hyperintensity was detected in 5/6 cases (83.33%). In 1 case,