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Intraventricular liponeurocytoma: The role of surgery and adjuvant therapy

D. Cannizzaro[a,b], C. Mancarella[a,b], D. Milani[a,*], B. Fernandes[c], M. Rossi[a], M. Fornari[a], A. Cardia[a]

[a] Department of Neurosurgery, Humanitas Clinical and Research Center, Rozzano, MI, Italy
[b] Department of Neurology, Psychiatry and Neurosurgery, Policlinico Umberto I, "Sapienza" University of Rome, Rome, Italy
[c] Department of Pathology, Humanitas Clinical and Research Center, Rozzano, MI, Italy

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ABSTRACT

Background: After a series of case reports, in the WHO classification of 2007, liponeurocytomas were reclassified as grade II tumors and confirmed in the last WHO classification of 2016. We describe a rare case of intraventricular location of liponeurocytoma with review of the literature and propose the management of these rare lesions.

Methods: We reviewed the pertinent english literature and extracted 9 articles to discuss 12 cases of intraventricular liponeurocytoma. We reported demographics and clinical data cases including our case.

Results: Patients mean age is 37 years. There is a male prevalence. All 12 patients underwent surgical treatment. A total tumor resection was obtained in 66,6%. There is one mortality reported due to intraventricular hemorrhage. In 4 cases K67/MIB-1 resulted < 1%, in 3 case it was 3–4%, and in 1 case it was 5%. Reoperation was performed in 3 cases due to reoccurance and regrowth.

Conclusions: The management of residual is still controversial in this tumor entity. Our analisys evidences the role of the radiotherapy in lesions with ki-67 index > 3% after subtotal removal.

1. Introduction

Liponeurocytomas are rare tumors characterized by the presence of small cytoplasmic lipid droplets. They are generally localized in the cerebellum [1]. The cerebellar liponeurocytoma is a "rare, well differentiated neurocytic tumor of the cerebellum that arises in adults and typically shows focal or regional lipomatous differentiation. It has a low proliferative potential and a more favorable prognosis especially when compared to medulloblastoma (MDB), from which it needs to be distinguished" as defined by the WHO [2]. Previously, these tumors were classified as adult lipomatous variant of medulloblastoma with much more benign clinical character than the common non-lipomatous medulloblastoma. Central neurocytomas have similar histology and immunoprofile except for the absence of fat component. Supratentorial intraventricular liponeurocytomas have been reported in the literature. Compared to the cerebellar location, those have not shown any calcification and have lacked lipid components [3].

Liponeurocytoma treatment is surgical total removal; adjuvant therapy is suggested in recurrent or residual lesions, especially when the proliferative potential (Ki-67 index) is high. In the literature a Ki-67 index is considered aggressive when > 5%.

We present a case of adult lyponeurocitoma of the fourth ventricle, diagnosed and treated in our department and compare the clinical and neuroradiological data of cases reported in the literature. We reviewed the pertinent literature, collecting 11 cases of intraventricular liponeurocyitomas; we analyzed all 12 cases (including the present case).

2. Case report

A 69-year-old woman presented to our institute with sudden coma after a 6 months-period of dizziness and progressive gait ataxia. Brain computer tomography (CT) was performed at admission in emergency department and a obstructive hydrocephalus was found. Brain magnetic resonance imaging (MRI) revealed a mass in the fourth ventricle, characterized by a hypodensity in T1-weighted series. T2-wighted and Flair MRI images showed a heterogeneous hyperintense lesion (Fig. 1).

The radiological characteristics of the lesion suggested an intraventricular tumor with differential diagnosis of ependymoma and medulloblastoma. Considering acute hydrocephalus causing coma, emergent surgery was indicated, and no informed consent was signed. Patient underwent to an external ventricular drainage; after the patient stabilized, we decided to immediately proceed with tumor removal and a suboccipital craniotomy with transvermian approach was performed to apporach the fourth ventricle. The tumor was completely resected

Abbreviations: CT, computer tomography; MDB, medulloblastoma; WHO, world health organization; MRI, magnetic resonance imaging; GFAP, glial fibrillary acid protein

* Corresponding author at: Via Alessandro Manzoni 56, Rozzano, Milano 20089, Italy.
E-mail address: davide.milani@humanitas.it (D. Milani).

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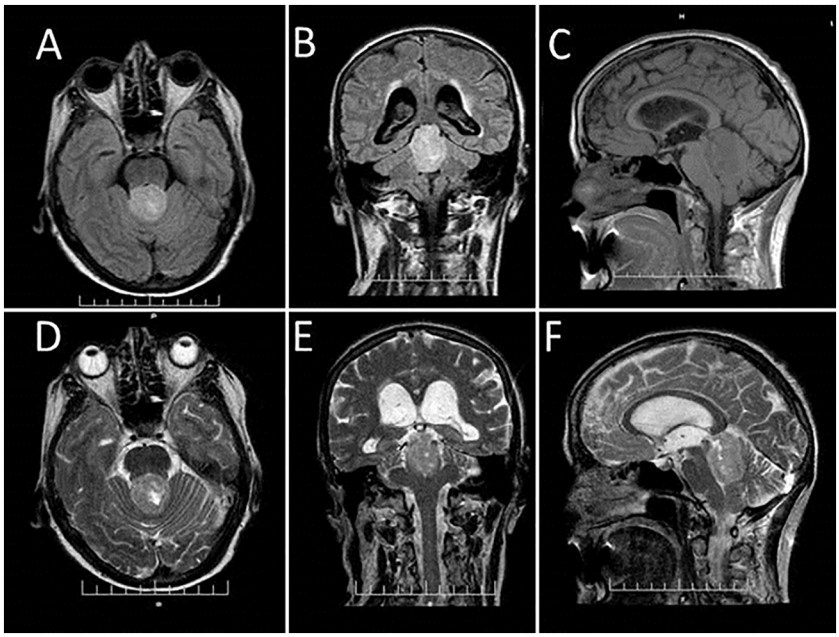

Fig. 1. Axial (A) and (B) coronal views of Flair MRI images show a lesion located in the fourth ventricle that appears hypointense on T1 weighted MRI image (showed in Sagittal view. C). On T2 weighted MRI images the lesion reveal heterogeneous and hyperintense features (axial, coronal and sagittal view D,E,F).

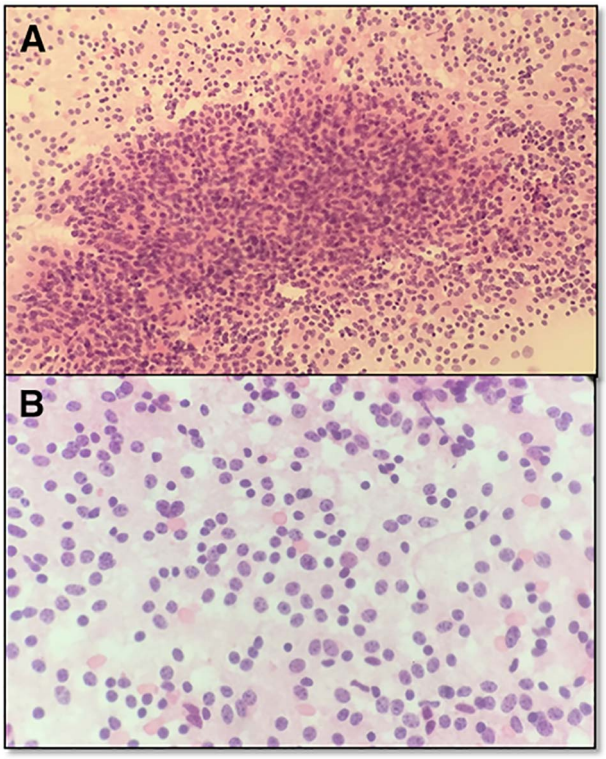

Fig. 2. Fresh frozen cytology: cytologic smears shows a monomorphic cell population, with rounded nuclei, without atipia. No mitotic figures are seen. (× 100) A and (× 200) B.

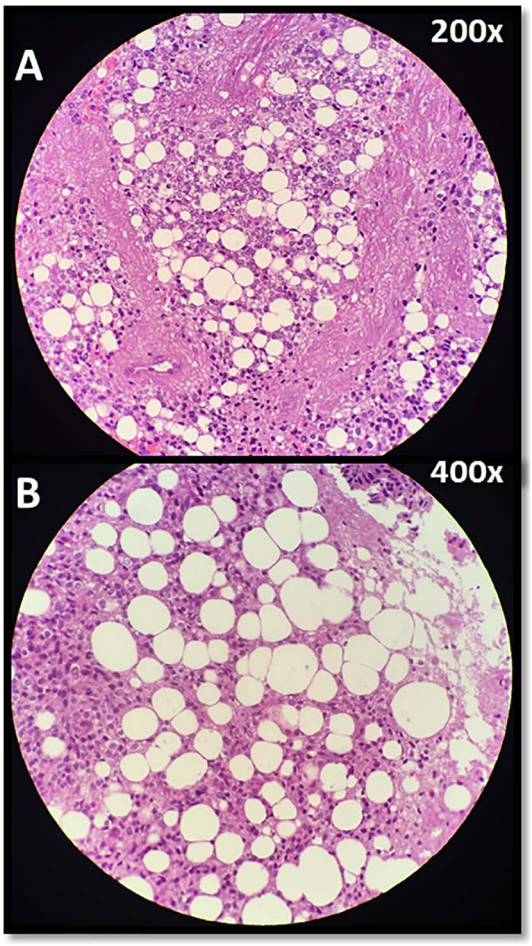

Fig. 3. Round-shaped tumor cells; with small, monomorphic nuclei and clear cytoplasm and small amount of adipocytes (× 200) A and (× 400) B. Hematoxylin and eosin staining.

and histological findings were suggestive of liponeurocytoma (WHO II). Neoplastic proliferation of round cells with smooth nuclear chromatin surrounded by neuropil mixed with a component of intracellular fat. The neoplastic population stained positively for synaptophysin and focally for fibrillary acid protein (GFAP). No evidence of mitotic figures, nor necrotic areas were found (Figs. 2, 3, 4, 5).

The physical examination, 24 h after the surgery evidenced paresis of IX cranial nerves, nystagmus in the right lateral gaze and general extremity weakness. 20 days later the patient underwent ventriculo-peritoneal shunt. 3 months later at the clinical follow up she was weakly ataxic. No radiotherapy or cheoterapy was performed and after 12 months the MRI didn't show a lesion recurrence after GTR (Fig. 6).

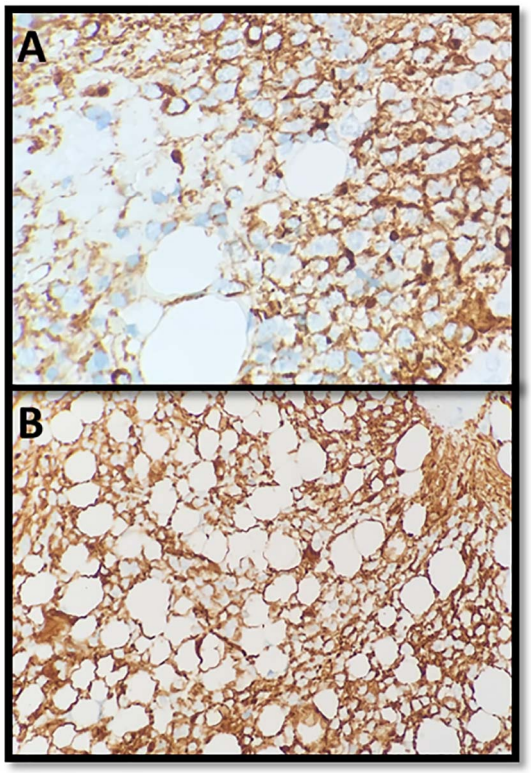

Fig. 4. Neoplastic cells in the tumor matrix, presence of perivascular glial cells highlighted by GFAP immunoreactions (A) with adipose tissue-like surrounded by positive GFAP immunostaining (B).

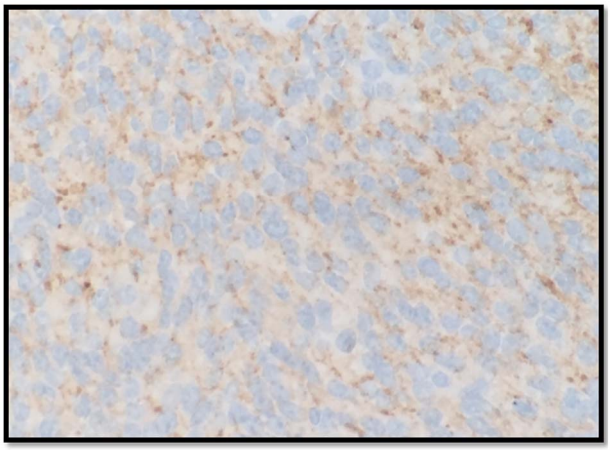

Fig. 5. Tumor cells expressing positive synaptophysin reaction.

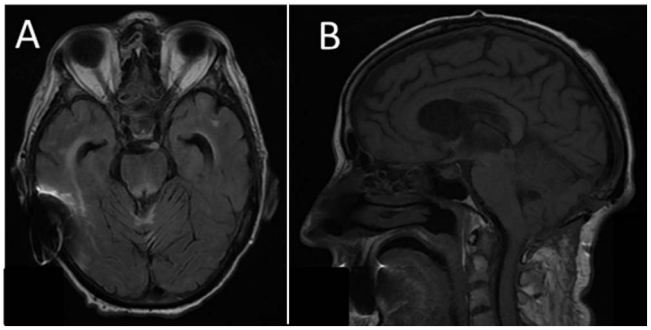

Fig. 6. Post-operative MRI (A and B) shows gross total removal of the liponeurocytoma.

2.1. Literature review

We conducted a systematic search for other cases of intraventricular liponeurocytoma using PubMed engine typing the following lemmas: liponeurocytoma, intraventricular, posterior cranial fossa.

We selected 9 english written articles describing liponeurocytoma's anatomopathological features, molecular aspects, WHO classification (from definition todate), location, collecting demographics and clinical data of 11 patients affected by intraventricular liponeurocytoma.

We include 12 patients (11 cases from the literatuere and 1 present case). The mean patients age is of 37 years (range from 4 to 59 years). There is a male prevalence, 8 Male, 4 Female (Table 1). All 12 patients underwent surgical treatment. A total tumor resection was obtained in 8 cases (66,6%), and in 4 cases (33,4%) a subtotal resection was accomplished. 1 patient (8,3%) died in third post-operative day due to intraventricular hemorrhage. In 4 cases K67/MIB-1 resulted < 1%, in 3 case it was 3–4%, and in 1 case it was 5%. In the 4 years old pediatric patient Ki67/MIB-1 resulted 10–15% at the first operation, the recurrene occured after 14 months and the Ki67/MIB-1 increased to 15–30%. Reoperation was performed in 3 cases, 2 patients who had a subtotal resection at the first surgical procedure (1 after 14 months and 1 after 64 months), and 1 patient who had a total resection at the first time showed recurrence at 108 months of follow up. This patient underwent radiotherapy after second surgical operation.

3. Discussion

Because of its rarity, little is known with regard to liponeurocytoma, especially supratentorial ones. In fact, a detailed review of the pertinent literature recognizes the lyponeurocitoma as mainly cerebellar lesion and reports few intraventricular cases.

In 1978 Bechtel et al. first described a cerebellar tumor compatible with a cerebellar liponeurocytoma [3]. Since that report, > 40 cases were reported in literature under different name as neurolipocytoma, medullocytoma, lipomatous glioneurocytoma, lipidized mature neuroectodermal tumor, and cerebellar liponeurocytoma and lipomatous medulloblastoma. In the 2000 the WHO classification recognized it as a nosological entity in the group of neuronal tumors. Liponeurocytomas were classified as neuronal and mixed neuronal-glial tumor of grade I, mostly because of the neurocytic differentiation and other name such as lipomatous medulloblastoma discouraged. After a series of case reports, in the WHO classification of 2007, liponeurocytomas were reclassified as grade II tumors and confirmed in the last WHO classification of 2016.

The most common location of the liponeurocytoma is in the cerebellar hemispheres. Its extension have been reported towards the pontocerebellar angle and the vermis; rarely also in the spinal location to C1–C2 [12,13]. One case of spinal lumbar metastasis occurring 11 years after initial diagnosis was reported [14].

Radiological diagnosis is difficult because of the rarity of the tumor and a variable imaging appearance. Usually these lesions appear heterogeneous on MRI scan, iso-, or hypointense on T1-weighted images, there are some areas of high signal intensity. These areas turn hypointense on fat suppression sequences. Contrast enhancement is usually present but irregular and heterogeneous; on T2-weighted images, the solid component is slightly hyperintense with focal evident hyperintense areas corresponding to fat. Usually there is no edema reported, but some cystic components may be present [12].

Immunohistochemical profile in liponeurocytomas is characterized by the positivity for synaptophysin, focally for fibrillary acid protein (GFAP) and for protein S-100. The K67/MIB-1 is usually < 1%, in case of higher value the probability of recurrence increases. Limaiem et al. reported that cerebellar liponeurocytomas recur when there were > 10% Ki-67-positive cells [15,16].

Surgery is recommended as the primary management, but there is no consensus on post-operative radiotherapy. In fact, the lack in understanding the tumor biological behavior led to different therapeutic

Table 1
Summary of literature review of intraventricular liponeurocytoma and total cases of our analysis.

	Sex	Age	Intraventricular location	Treatment	Removal	K67/MIB-1	Follow-up	Recurrence	Retreatment	Adjuvant therapy
Horoupian, 1997 [7]	M	30	Lateral v., 3rd v	Surgery	Subtotal	–	5 months	N	–	N
George, 2001 [5]	F	59	Lateral v.	Surgery	Subtotal	5%	67 months	Y	Surgery	N
Rajesh, 2003 [11]	M	30	Lateral v.	Surgery	Gross total	–	Died for intraventricular bleeding	–	–	
Jouvet, 2005 [8]	F	4	4th v.	Surgery	Subtotal	10–15%	14 months	Y	Surgery	N
Kuchelmeister, 2006 [9]	M	35	Lateral v.	Surgery	Subtotal	4%	–	–	–	–
Pankaj, 2010 [10]	M	35	Lateral v.	Surgery	Total	–	–	–	–	–
Gupta, 2011 [6]	F	45	Trigone of Lat. v.	Surgery	Total	3%	10 months	N	–	N
Chakraborti, 2011 [4]	M	36	Lateral v	surgery	Total	3–4%	108 months	Y	Surgery	Y Radiotherapy after second surgery (no recurrence at 2 years fu)
	M	30	Lateral v.	Surgery	Gross total	< 1%	Lost	–	–	N
	M	32	Lateral v., 3rd v.	Surgery	Gross total	< 1%	Lost	–	–	N
Karabagli (2014) [2]	M	34	Lateral v., 3rd v., 4th v.	Surgery	Gross total	1,5%	24 months	N	–	
Present case	F	69	4th v.	Surgery	Total	< 1%	12 months	N	–	

lines. Based on our literature review, radiation should be recommended when residual tumor is present or a high Ki-67. Current guidelines on cerebellar liponeurocytoma recognize surgical treatment of choice with total surgical removal as a goal and long-term follow up, the role of radiotherapy is reserved to recurrent tumor and in subtotal removal with ki-67 index > 5% [14,17]. Liponeurocytoma is considered to have low proliferative potential when the MIB-1/Ki-67 proliferation index is < 2%–3% [1]. In our review series of intraventricular liponeurocytoma, the recurrence after surgery, occurred in cases with value of ki-67 index ≥ 3%.

Due to the rarity of the tumor this review is limited to only 12 cases, so we cannot define a guideline of management but we suggest, in pure intraventricular liponeurocytoma, to consider adjuvant radiotherapy after subtotal removal or when the ki-67 index is > 3%.

4. Conclusion

Liponeurocytoma is a rare intracranial tumor, with exceptional intraventricular location. Complete surgical removal is recommended. The correct management of residual is not clear. Our analisys evidences the role of the radiotherapy in lesions with ki-67 index > 3% after subtotal removal.

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