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Case Report

A case of adult cerebellar liponeurocytoma with atypical radiological features and long survival with literature review

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ABSTRACT

Cerebellar liponeurocytoma or lipomatous medulloblastoma is a rare oncological entity. Knowledge regarding the management and outcomes of these rare tumors are still evolving. Very few cases have been described previously in the literature. The authors report a case of a middle-aged woman operated on twice, 8 years apart, with uneventful postoperative follow-ups. Radiological characteristics were revealed atypically on the computed tomography scan and magnetic resonance imaging. Histopathological study supported a cerebellar liponeurocytoma with classic immunohistochemical features. Through this report, the authors aim to describe atypical radiological and histopathological features of this rare entity with good outcome by going through a comprehensive review of the existing literature.

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Introduction

Cerebellar liponeurocytoma, initially called lipomatous medulloblastoma, is a rarely encountered tumor, first reported by Bechtel et al. in 1978 in a 44-year-old man, thus referring to his markedly better prognostic nature [1]. Since then, several authors have reported it using different nomenclatures as follows: neurolipocytoma, [2] medulloctoma, [3] lipid medulloblastoma, [4] and glioneurocytomelipomatous [5].

Later, in the World Health Organization's classification (WHO 2000), this tumor was designated as a separate grade I entity. However, due to its multiple reported recurrences and atypical features, it subsequently reached grade II according to the new WHO classification updated in 2007 and recently in 2016 [6,7,22]. The authors report through this work a case of cerebellar vermis liponeurocytoma in a 44-year-old woman operated on twice with a follow-up of more than 8 years after surgery as well as a comprehensive literature review of the previously reported cases.

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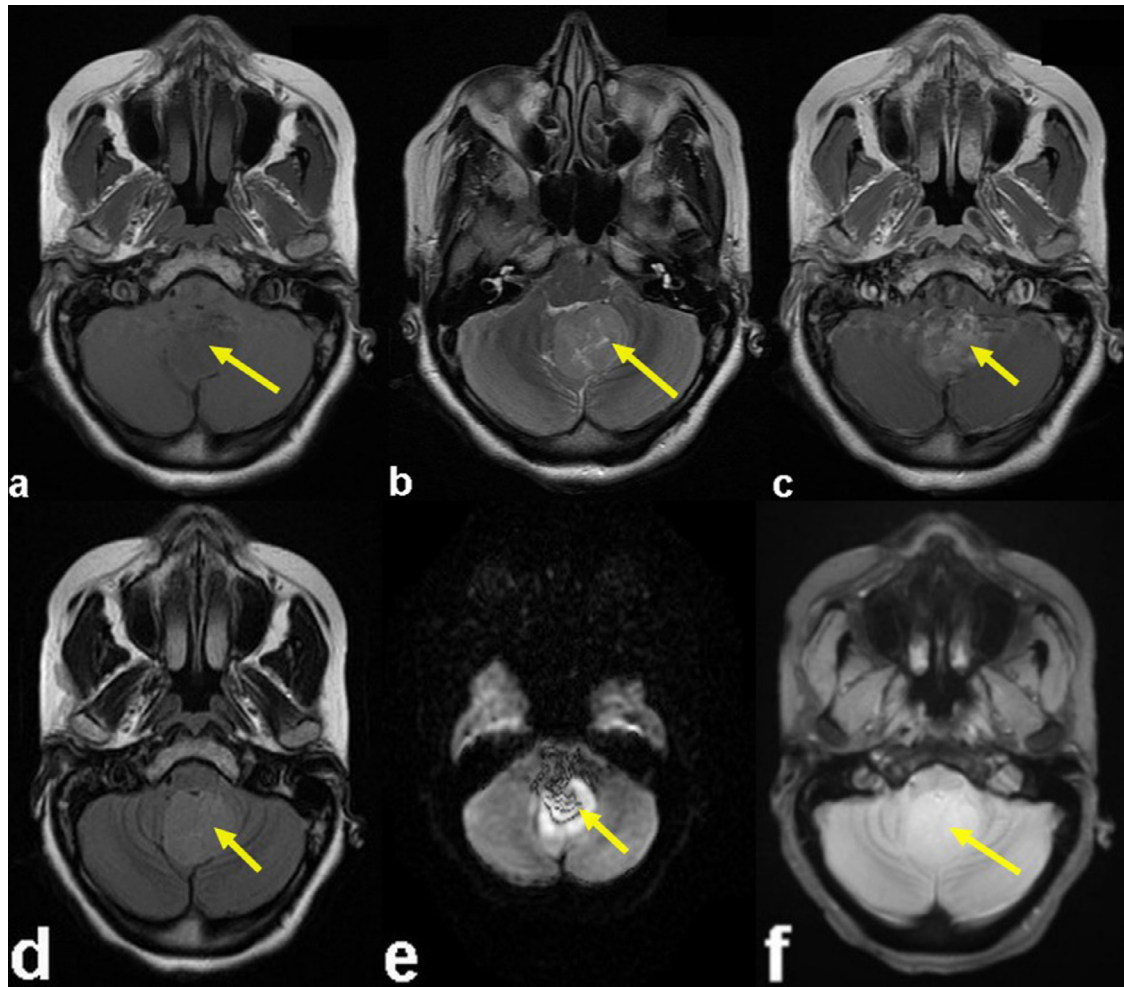


Fig. 1 – Brain magnetic resonance imaging (MRI) in axial imaging planes showing an inferior median oval cerebellar vermis lesion (yellow arrows) measuring 40 × 31 × 29 mm in diameter with hypointense T1 signal (A) and heterogeneous T2 hypersignal (B) which is enhanced heterogeneously after injection of Gadolinium chelates (C). It exerts a mass effect on the bulb and fills the Magendi's hole as well as the occipital foramen. No surrounding edema the lesion is seen on Fluid-attenuated inversion recovery (FLAIR) imaging. Diffusion-weighted imaging (DWI) showed an increased signal (E) but there was no bleeding or calcification on the GRE T2*-Weighted sequence (F).

Case report

This is a 44-year-old lady who had been operated on for a simple mammary cyst and who was admitted for an intracranial hypertension syndrome made up of severe occipital and temporal headaches dating from 4 months of rapidly progressive onset progressing from paroxysmal, worsened by changes in position and associated with bilateral blurry vision and morning projectile vomiting. Neurological examination revealed kinetic and static cerebellar syndrome made of ataxia, imbalance, uncoordinated movements, and oculomotor disorders made of bilateral nystagmus with two-sided stage I papilledema. Brain computed tomography (CT) scan was found to be without abnormalities. Brain magnetic resonance imaging (MRI) (Fig. 1) showed an inferior median oval cerebellar vermis lesion measuring 40 × 31 × 29 mm in diameter with hypointense T1 signal and heterogeneous T2 hypersignal which

was enhanced heterogeneously after Gadolinium chelate injection. This lesion exerted a mass effect on the bulb and fills the Magendi's hole as well as the occipital foramen. Magnetic resonance spectroscopy showed an increase in the choline peak and a drop in the peak of N-acetyl aspartate. The patient underwent surgery in the prone position with her head in hyperflexion and held by the Mayfield skull clamp. We performed two small burr holes below the nuchal line, 3 to 4 cm from the midline after exposure of the squamous part of the occipital bone. From these burr holes, we proceeded either with a kerison towards the contralateral side and then down to the foramen magnum. We created, thus, a rectangular craniotomy. The dura was incised in a "Y"-shaped manner and its shreds were hung. A subtotal tumor resection with a transvermian approach was performed. No neuromonitoring or neuronavigation were performed and the bone flap was replaced in place by the end. The postoperative course was uneventful with only persistent gait disorders.

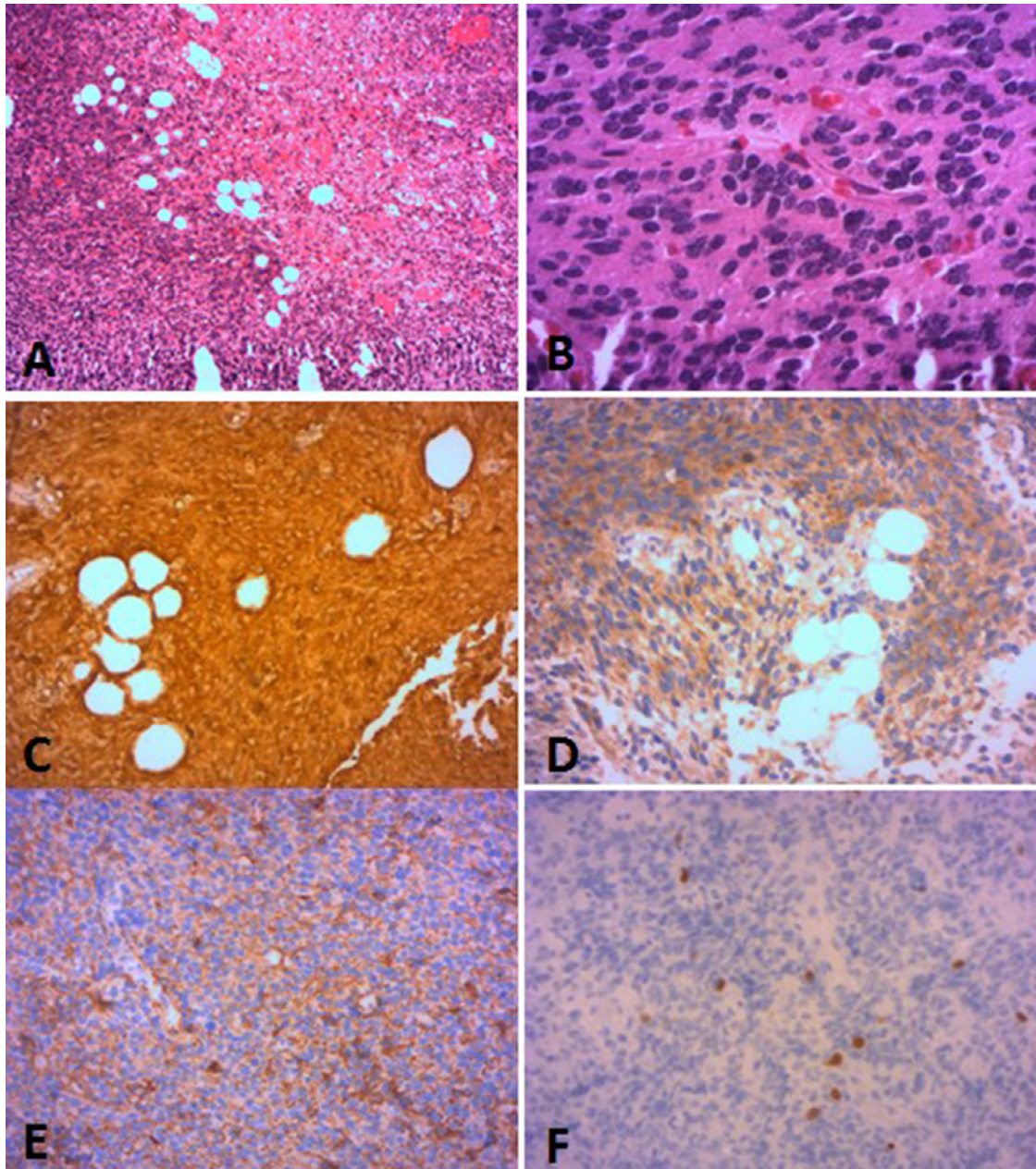


Fig. 2 – Histopathological examination of the specimens showing dense cell proliferation associating small monomorphic cells and fat cells characterized by optically empty vacuoles (A) (HE \times 100). Predominant tumor cells with poorly visible cytoplasm and fairly monomorphic round or ovoid nuclei (B) (HE \times 200). Expression by tumor cells of NSE (C), synaptophysin (D) and focal GFAP (E) (\times 200) with 5% Ki-67 proliferation index (F) (\times 200).

Histological examination through Hematoxylin-and-eosin-stained sections (Fig. 2) revealed moderate tumor proliferation involving two contingents. The main one was made of cells distributed in a fibrillar background, with poorly visible cytoplasm and fairly monomorphic round or ovoid nuclei. The second contingent was made of adipose cells characterized by optically empty vacuoles. Mitoses were exceptional. No necrosis was observed. Immunohistochemical study showed the expression of neuron specific enolase (NSE) and synaptophysin by both cell types. The glial fibrillar acid protein (GFAP) was expressed by rare tumor cells and rare

reactive astrocytes. The proliferation index evaluated using the Mindbomb 1 (MIB1) antibody was measured at 5%. The diagnosis of liponeurocytoma was thus retained.

Our patient was lost to follow-up for 8 years, during which time she had no x-ray examination. After this entire period, she comes back for recurrence of the gradually worsening intracranial hypertension syndrome with gait disturbances. Neurological examination revealed static and kinetic cerebellar syndrome associated with stage I bilateral papilledema. Cerebral and full spine MRI (Fig. 3) showed an expansive cerebellar vermis tumor reaching the left cerebellum

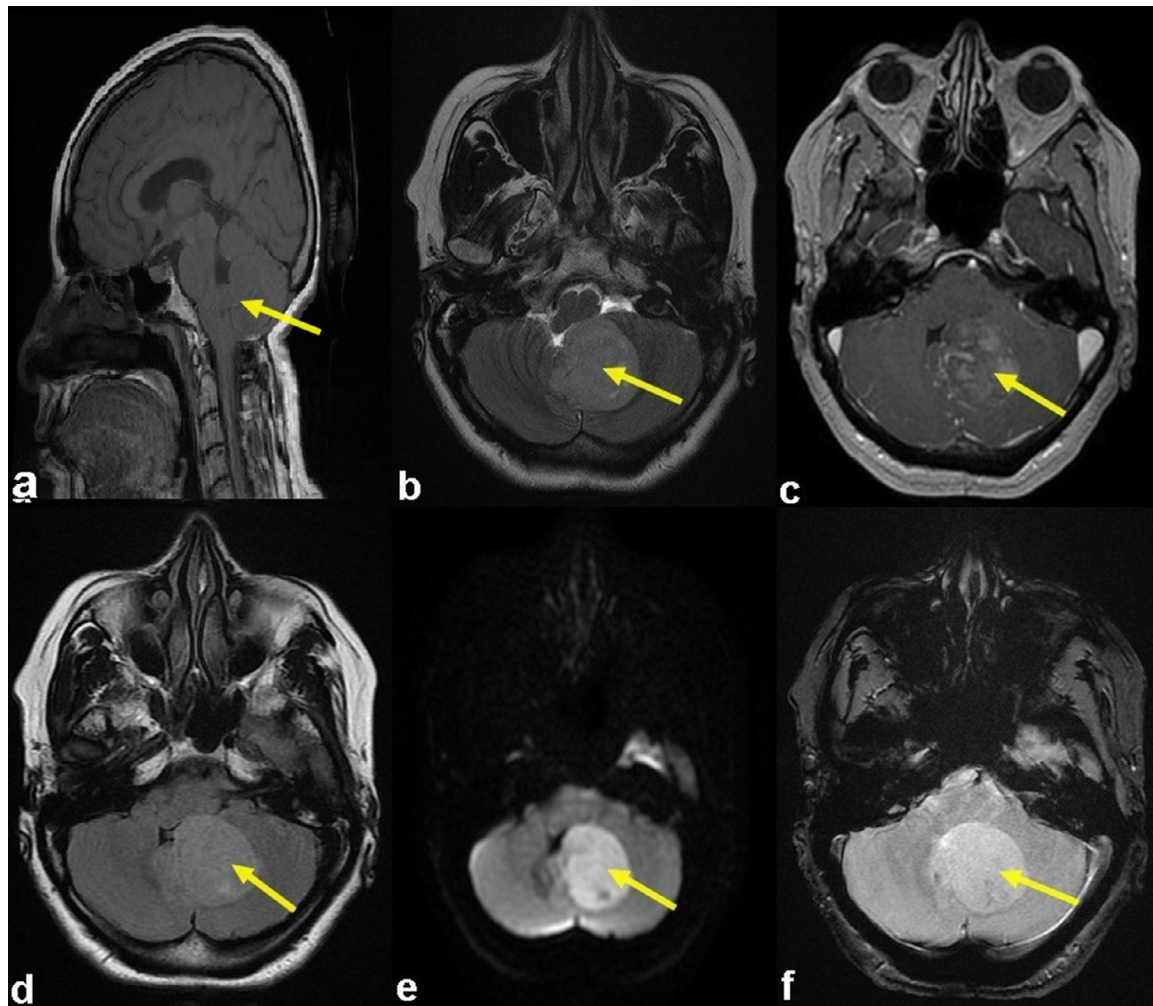


Fig. 3 – Brain magnetic resonance imaging (MRI) in sagittal and axial imaging planes showing the recurrent expansive cerebellar vermis tumor (yellow arrows) reaching the left cerebellum (37 × 36 × 35 mm in diameter) extended to the fourth ventricle and to medulla oblongata made of hypointense signal on T1 weighted sequence (A) and heterogeneous signal on T2 weighted image (B) with restricted signal on diffusion-weighted imaging (DWI) (E). The tumor was heterogeneously enhanced after injection of Gadolinium chelates (C) without surrounding edema (C) or bleeding or on the GRE T2*-weighted sequence (F).

(37 × 36 × 35 mm in diameter) extended to the fourth ventricle and to medulla oblongata made of heterogeneous signal on T2 weighted image seat of some cystic areas and which was hypointense on T1 weighted sequence with restricted signal on diffusion-weighted imaging (DWI) and heterogeneously enhanced after injection of Gadolinium chelate. There were no signs of spinal cord extension or bleeding. The patient underwent surgery by the same suboccipital approach in prone position with head in hyperflexion and held by the Mayfield skull clamp, having undergone incomplete resection of a friable but non suckable hemorrhagic lesion on contact. The postoperative follow-up was uneventful. Histopathological examination of the surgical specimen showed histological appearance similar to that of the old tumor, but with a higher percentage of fat cells (Fig. 4). We therefore concluded that her liponeurocytoma had recurred eight years after the first surgery. Our patient was lost unfortunately again to follow-up so that she did

not perform postoperative imaging. She presented 8 months later, after receiving brain radiation therapy at a dose of 54 Gray delivered in 1.8–2.0 Gray fractions over 8 weeks, with a new brain MRI showing a median cerebellar vermis tumor residue (yellow arrows) measuring 42 × 52 × 40 mm in diameter with hypointense T1 signal and heterogeneous T2 hyper-signal with moderate enhancement after injection of Gadolinium chelates. This residue was filling the lower part of the fourth ventricle, which was dilated, with posterior extension towards the craniectomy flap without affecting the soft tissues. No surrounding peritumoral vasogenic edema was seen on Fluid-attenuated inversion recovery (FLAIR) imaging. DWI sequence showed an increased signal with no bleeding on the GRE T2*-Weighted sequence. There was no leptomeningeal contrast enhancement on the medullary level.

Fig. 5.

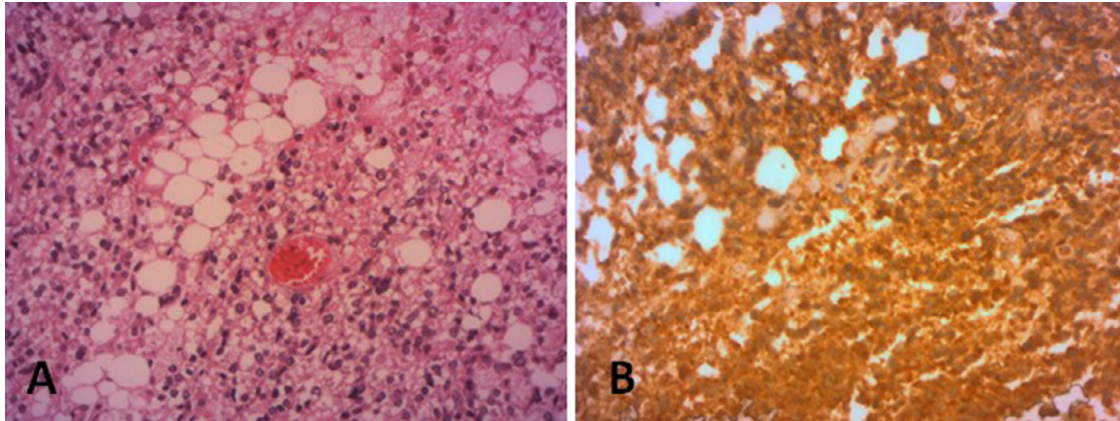


Fig. 4 – Photomicrograph of the last specimen from the recurrent tumor showing moderate density cell proliferation associating small monomorphic cells and fat cells (A) (HE \times 100). Expression of NSE by tumor cells (B) (\times 200).

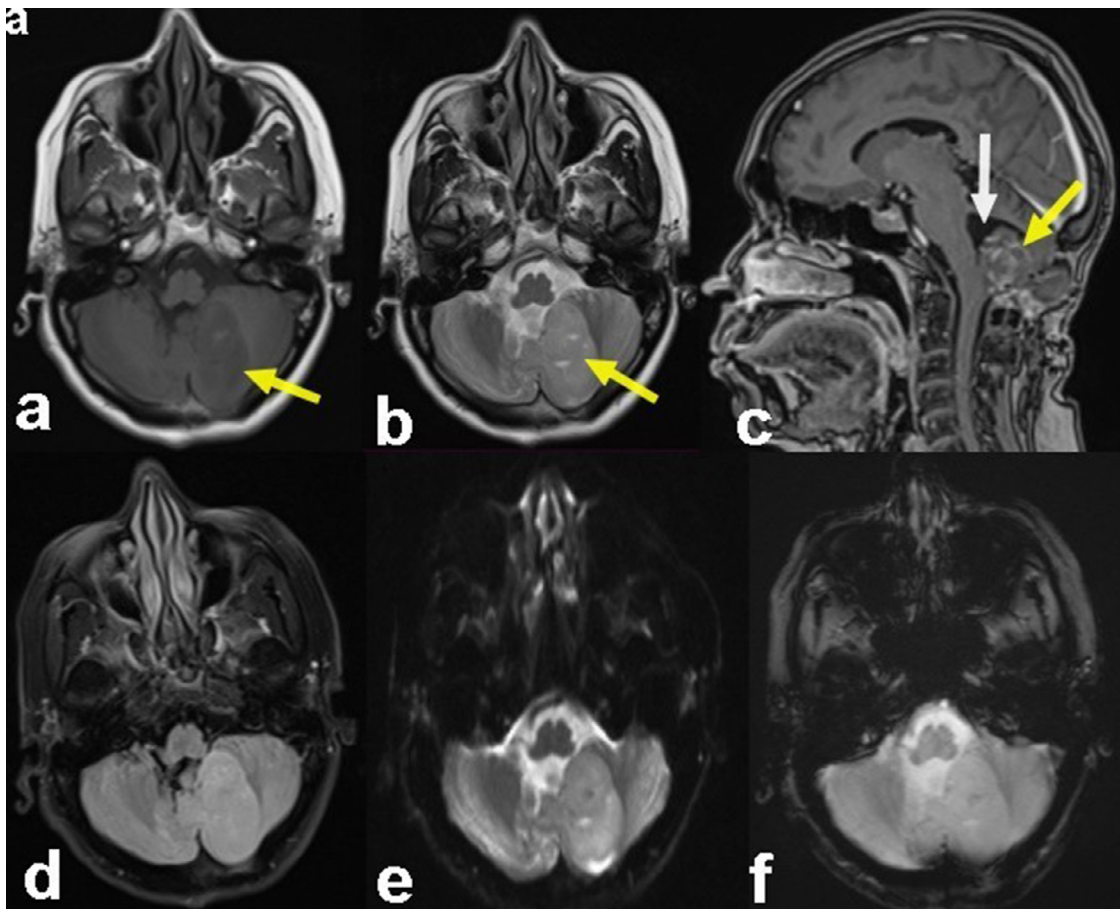


Fig. 5 – MRI at 8 months postoperatively and after brain irradiation in axial planes showing a new recurrent median oval cerebellar vermian tumor residue (yellow arrows) measuring 42 \times 52 \times 40 mm in diameter with hypointense T1 signal (A) and heterogeneous T2 hypersignal (B) with moderate enhancement after injection of Gadolinium chelates (C; sagittal plane). Note the filling of the lower part of the fourth ventricle, which is dilated (C; white arrow), and the posterior extension towards the craniectomy flap without affecting the soft tissues. No surrounding peritumoral vasogenic edema is seen on Fluid-attenuated inversion recovery (FLAIR) imaging (D). Diffusion-weighted imaging (DWI) showed an increased signal (E) with no bleeding on the GRE T2*-Weighted sequence (F).

Discussion

In 2013, Oudrhiri et al, in their report, examined 36 cases of liponeurocytomas cited above and found that the mean age of onset of this lesion was 49 years (range 32–79 years) with a female preponderance (1, 8/1) [8]. Recent reports also exist in the form of individual cases, the most common being infratentorial localization [9,10,11,12,13,20]. The predominant clinical manifestation was related to the symptoms of the posterior cerebral fossa, all patients presented with signs of cerebellar dysfunction [12,13]. The starting complaints, in decreasing order of frequency, were headaches, gait disturbance, and visual impairment. All these signs were present in our case during both hospitalizations. The lesions often reach more than 4 cm before their clinical presentation. The symptomatic recurrence period, if it occurs, after subtotal resection is generally long, reaching 7 years in our case. However, once symptomatic recurrence occurs, the period between subsequent procedures is usually much shorter [12,13].

In a systematic review of all previous cases (n = 73) up to 2018, Gembruch et al. noted that these tumors had a low MIB-1 proliferation index ($3.73 \pm 4.01\%$) [14]. Among infratentorial locations, cerebellar hemisphere is the most common and most frequent location [15, 16,17]. Spinal extension at C1 - C2 level [16,18] as well as one case of spinal lumbar metastases occurring 11 years after initial diagnosis have been previously reported [15].

Central neurocytomas can be considered as differential diagnosis, although they usually do not have lipomatous components. The fatty component of liponeurocytoma may be detected on CT scan having hypodense aspect. In our case, CT scan was strictly normal on admission and did not show any lipid component. MRI will reveal the hyperintense lesion on T1-weighted sequences, which is reversed in fat-suppressed sequences [16]. These findings, although not given initial attention, can be understood retrospectively after histological diagnosis. As a result, awareness of this rare entity, a clear understanding of the characteristics of MRI and the presence of fat within the lesion will make it possible to make the diagnosis even preoperatively. In our case, the lesion did not express these characteristics on MRI since it appeared hypointense on T1 sequence and hyperintense on T2 and therefore the fatty component was not revealed preoperatively on imaging. These tumors must be differentiated from medulloblastomas and ependymomas, which may rarely express T1 hyperintensity [16,20]. Histologically, medulloblastoma in its classic form can show foamy histiocytes with primitive neuroectodermal cells. However, a high proliferation index will clearly indicate the malignant nature of the tumor. As one can probably understand, differentiation between these entities is essential for decision-making.

In recent reports [10,11], familial predisposition has been suggested with possibly an autosomal dominant mode of inheritance. However, causal genetic mutation as well as the cell of origin of liponeurocytoma has yet to be determined. Some findings are now associated with liponeurocytomas and their heredity. A NEUROG1 gene transcription associated with the absence of the ATOH1 transcription factor were reported by Anghileri et al. [17]. In both cases of cerebellar liponeu-

rocytoma, they also noted overexpression of the 4 fatty acid binding protein. These results led the authors to conclude that liponeurocytoma could be the consequence of transformation of the cerebellum progenitor cells into adipose tumor cells by a possible aberrant differentiation. These are different from the cerebellar granular progenitor cells that were initially thought to be the origin cell of these tumors [17,19,21]. Wolf et al. suggested a germline mutation predisposing to the onset of liponeurocytomas [11]. Germline mutations are generally seen in gene with a proven role in oncogenesis, and such an understanding would be beneficial for other family members to determine their risk of such tumor occurrence.

However, optimal treatment option continues to be surgical. Given the low proliferation index (<5%) reported by most authors, radiotherapy does not appear to be a relevant option. Gembruch et al. reported tumor recurrence in 8.33% of cases after adjuvant radiotherapy. This contrasts sharply with the recurrence rates observed in cases that did not undergo radiotherapy (13/29 or 44.83%) [14]. Regarding the medullary level, there have been no reports of spinal fluid metastases in the literature and it is therefore reasonable to avoid spinal radiation. This also applies to our case since the postoperative cerebral and full spine MRI did not show any evidence of extension to the spinal cord. However, indications for considering adjuvant therapy in an individual case do not seem clear, bearing in mind the benign nature of the tumor. A lack of knowledge of the natural history of the tumor contributes to such gaps in our understanding and does not allow drawing a clear management strategy.

Management of recurrence should be specific to the patient with recurring symptoms or significant lesion growth requiring surgery. Since the longest reported survival was 18 years in 2 patients [15,16], a slow growth rate can be assumed, and therefore observation of “silent” recurrences is recommended. Thus, there is a need to report and monitor these cases to better understand this rare entity and to establish guidelines for treatment.

Conclusion

The small number of cases of cerebellar liponeurocytomas limits our understanding of the natural history of this tumor. Most of the knowledge available in previously reported cases indicates that this lesion is less aggressive than typical medulloblastomas. Its radiological features are uncommon. The low mitotic rate, the absence of metastases, and the long survival in several patients who have not received any adjuvant treatment indicate a less aggressive course and better prognosis.

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Competing interest

The authors declare that there are no conflicts of interest including financial, consultant, institutional and other relationships that might lead to bias or to a conflict of interest.

Patient Consent

Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

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