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CASE REPORT

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Meningioangiomatosis with meningioma: an uncommon association of a rare entity—report of a case and review of the literature

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Abstract *Introduction:* Meningioangiomatosis (MA) is a rare lesion, probably of malformative origin, consisting of meningovascular proliferation and leptomeningeal calcification. Patients with MA usually present with seizures or persistent headaches. Neurofibromatosis may be associated in a variable proportion of patients, while in others it may be sporadic. Surgical treatment is usually recommended, and is gratifying in most cases. Rarely, MA has been described coexisting with meningiomas, arteriovenous malformations, encephaloceles, oligodendrogliomas, meningeal haemangiopericytomas and orbital erosion. Among these, meningiomatosis with meningioma is the most frequent combination. *Case report:* We report a case of MA with meningioma in an 18-month-old girl, who presented with recurrent seizures. *Discussion:* In these situations, it is extremely important for the pathologist to be aware of this entity and to distinguish it from other lesions, like cortical invasion by a meningioma, intraparenchymal meningioma and intracerebral schwannoma, which it may mimic.

Keywords Meningioangiomatosis · Meningioma · Neurofibromatosis · Epilepsy · Children

Introduction

Meningioangiomatosis (MA) is a rare, benign hamartomatous lesion of the central nervous system. It usually presents as a plaque-like or nodular mass within the cerebral cortex and overlying leptomeninges, although rare cases in the thalamus and brain stem have also been described. MA occurs both in patients with neurofibromatosis (mainly type 2; NF-2), as well as in sporadic cases. Patients may be entirely asymptomatic, especially those with NF-2, unlike in sporadic cases, which frequently present with a long history of seizures and/or headache [5].

Histopathologically, it is characterised by cortical meningovascular proliferation and leptomeningeal calcifications. In some cases the lesion may show perivascular proliferation of elongated spindle-shaped cells trapping islands of gliotic-appearing cortex, which may be erroneously interpreted as tumour invasion by those who are not familiar with this condition. Despite almost 60 cases of this condition having been described so far, the histogenesis of these lesions is still unclear. The lesion has been variously described as a vascular malformation, hamartoma, neoplasm or metaplasia. The cell responsible is also thought variously to be a meningothelial cell, fibroblast or perivascular connective tissue cell [17].

The combination of a meningioma occurring together with MA in the same patient is quite rare, and only 16 cases have been reported in the English literature to date [1, 3, 4,

7, 8, 11–13, 15, 18]. We report here another case of meningioangiomatosis with an associated meningioma in a young child, who was treated at our institution.

Case report

The patient, an 18-month-old girl, started having recurrent, secondarily generalised seizures from the age of 1 year. The episodes were either with a right-sided focal motor onset or with complex bilateral motor phenomenon prior to generalised tonic–clonic movements. The seizure frequency was on average five per day, despite treatment with multiple anti-epileptic drugs, and the child had developmental delay from the time she started having seizures. With this background, she was referred to our centre for surgical treatment for her intractable epilepsy. Her IQ was found to be 40, and the EEG and video-EEG showed a predominantly left-sided temporal seizure focus, with a few events not showing any focal onset.

Neuroimaging findings

The CT scan showed an enhancing lesion in the left temporal lobe, medial and anterior to the uncus. It was superficial in location and along the meninges (Fig. 1a). Besides the meningeal lesion, the contrast-enhanced CT revealed an additional intraparenchymal enhancing lesion in the temporal lobe (Fig. 1b).

The MRI revealed a discrete low-signal area in the left medial temporal region, which was isointense to the brain on the T1-weighted image (Fig. 1c). On the T2-weighted image the lesion was hyperintense, without any demarcation of the extraparenchymal lesion from the intraparenchymal pathology (Fig. 1d). The possibility of a low-grade glial neoplasm was considered.

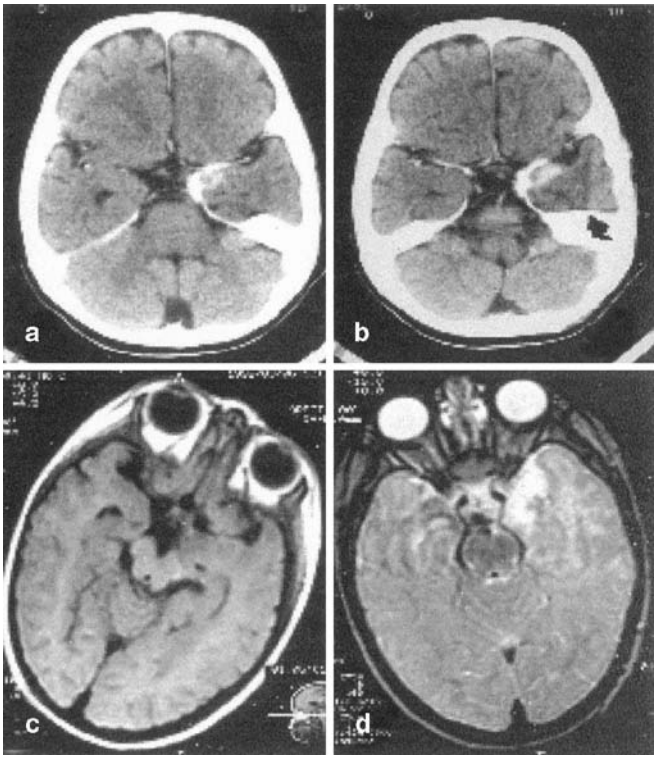

Fig. 1 **a** CT scan. An enhancing lesion in the temporal lobe medial and anterior to the uncus, located superficially along the meninges. **b** Contrast-enhanced CT. Focal intraparenchymal enhancing lesion seen in the temporal lobe, in addition to the meningeal lesion. **c** T1-weighted MRI. The lesion is isointense to the brain. **d** T2-weighted MRI. The lesion is hyperintense without any differentiation of the extraparenchymal lesion from the intraparenchymal pathology.

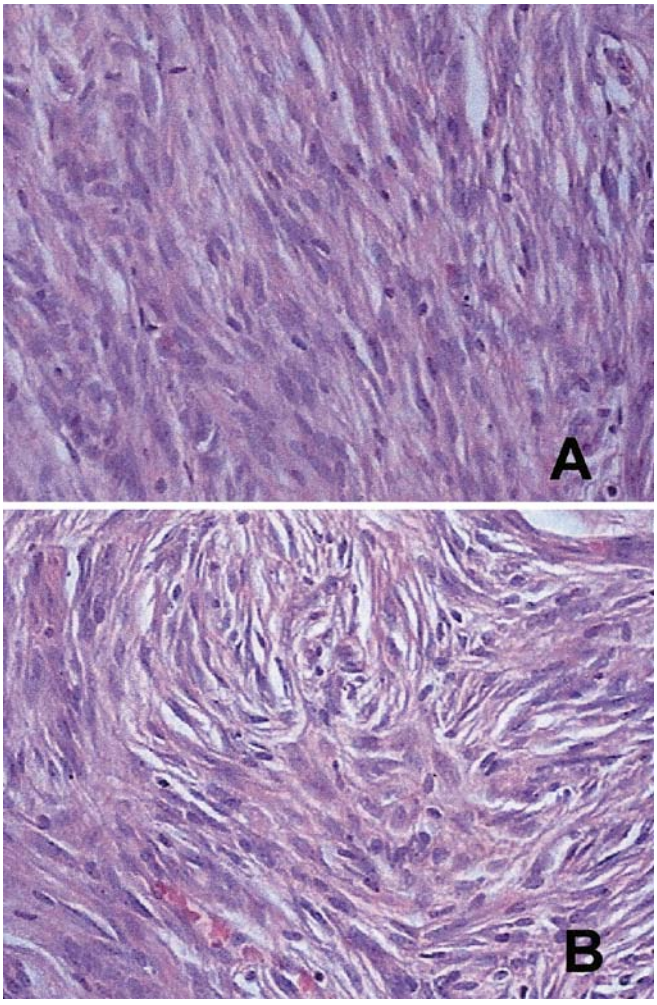

Fig. 2 Photomicrographs of the transitional meningioma area (**a** H&E, ×200 and **b** H&E, ×200)

Operative intervention and findings

At surgery, a firm lesion was found in the left medial temporal cortex, which was well circumscribed and associated with another dural-based lesion, which appeared to be similar to an en-plaque meningioma carpeting the sphenoid ridge and the medial aspect of the middle cranial fossa. Total excision of the cortical lesion and subtotal excision of the dural lesion was carried out, and the disappearance of spike discharges was documented intraoperatively after excision using electrocorticography (Nihon-Kohden Electroencephalograph 2100).

Histopathological examination

Microscopic examination of the dural-based lesion showed elongated cells arranged in interwoven fascicles and whorls, with occasional psammoma bodies. This picture was consistent with the diagnosis of transitional meningioma (Fig. 2).

Sections examined from the cortical lesion revealed numerous small intracortical blood vessels, which were ensheathed by spindle-shaped meningothelial cells and fibroblasts in cuffs and parallel bundles. In sections taken perpendicular to the axes of blood vessels, the ensheathing cells had an 'onion-peel' appearance. There was no nuclear pleomorphism or mitosis. Scattered minute calcification was identified. The intervening cortical parenchyma showed enlarged reactive astrocytes associated with gliosis (Fig. 3a–d).

Immunohistochemical study revealed these cells to be positive for epithelial membrane antigen (EMA) and vimentin, but negative for glial fibrillary acidic protein (GFAP) and S-100. MIB-LI (MIB1 labelling index) was nil, and the cells were immunonegative for p53.

Postoperative course

Postoperatively, this patient developed a transient mild right hemiparesis. The patient had infrequent seizures for the first 8 months after surgery, after which she did not have any seizures for the rest of her total follow-up of 4 years. Follow-up MRI did not reveal any residual medial temporal lesion, although it showed a stable residual dural thickening along the medial aspect of the middle cranial fossa.

Discussion

Meningioangiomatosis was first described by Bassoe and Nuzum [2] in 1915 as an incidental autopsy finding in a 15-year-old boy with neurofibromatosis-2 (NF-2). Subsequently Worster-Drought et al. [19] described a similar case in 1937, and named it 'meningioangiomatosis'. To the best of our knowledge, 60 such cases have been reported in the English-language literature [16], the majority being autopsy reports in patients with NF-2 [2, 5, 17, 19]. However, Takeshima et al. [16] observed this association in only 25% of their patients, while in the remaining 75% it occurred only sporadically.

Rarely, MA has also been reported to coexist with meningiomas, arteriovenous malformations, encephaloceles, oligodendrogliomas, meningeal haemangiopericytomas and

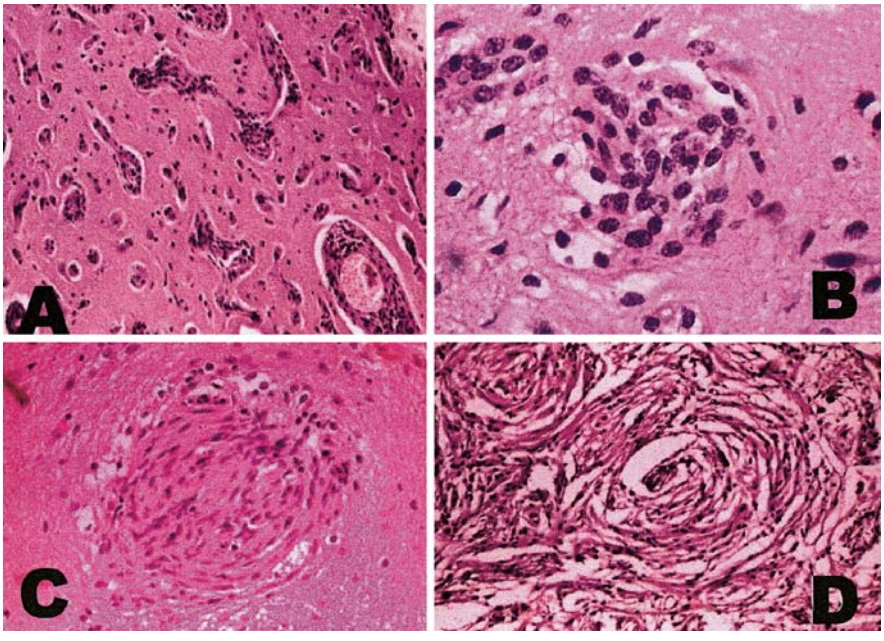

Fig. 3 Photomicrographs of the meningioangiomatosis area showing numerous small intracortical blood vessels ensheathed by spindle-shaped meningothelial cells and fibroblasts (**a** H&E, ×200; **b** H&E, ×400; **c** H&E, ×200). In one focus, the ensheathing cells had an 'onion-peel' appearance (**d** H&E, ×200).

orbital erosions [8]. Although MA with meningioma is the most frequent combination, only 16 cases have been documented to date [1, 3, 4, 7, 8, 11–13, 15, 18]. Most of these are single case reports, while the largest series by Kim et al. [8] consisted of five cases. None of these had any association with NF-2 (Table 1). We have analysed the data of all these 16 dual lesions and compared them with the features seen in solitary MA cases.

The age distribution of MA patients ranged from 9 months to 70 years (average age 28 and 21 years with and without NF-2 respectively) [16, 17], unlike MA with meningioma, which typically affects a younger age group, ranging from 11 months to 33 years (mean 13.3 years; Table 1).

Cases of MA with or without associated meningioma show a 2- to 3-fold male preponderance (unlike conventional meningiomas) [7, 17], with predilection for the frontotemporal cortex (Table 1) [6, 11]. Rarely, MA has also been reported to occur in the diencephalon [5], brain stem [10] and outside the cerebral cortex [13, 15]. Both groups of patients usually present with seizures that progress to becoming intractable (Table 1) [1, 3, 4, 7, 8, 11–13, 15, 18]. Other clinical manifestations are in the form of headache, facial pain and lower cranial nerve palsies. A large group of patients with MA, especially those associated with NF-2, however, remain clinically asymptomatic, and are diagnosed incidentally on autopsy [5, 17].

Meningioangiomatosis does not have a typical appearance on imaging [17]. CT generally shows a round, hypodense mass with varying degrees of calcification in the cortical leptomeningeal area, with little or no contrast enhancement. MR findings are also confined to the cortex,

Table 1 Cases of meningioangiomatosis associated with meningioma. *T-O* temporo-occipital, *F-P* frontoparietal, *NR* no recurrence, *FU* follow-up

Study	Site	Age (years)/ sex	Clinical presentation	Duration of symptoms	Type of meningioma	Clinical outcome
[1]	Frontal	15/male	Symptoms of subarachnoid haemorrhage	Not recorded	Fibroblastic	Dead due to operative complication
[11]	Frontal	15/male	Signs and symptoms of subarachnoid haemorrhage	1 year	Fibroblastic	Not recorded
	Frontal	33/male	Supraorbital headache	2 years	Transitional	Not recorded
[18]	Frontal	17/male	–	–	Transitional	Not recorded
[3]	Frontal	11 months/ male	Focal seizure	Not recorded	Transitional	No recurrence
[4]	T-O	9/male	Asymptomatic; investigated for mild head trauma	Not recorded	Transitional	No recurrence
	Frontal	28/male	Intractable seizures	2 years	Transitional	2 years FU/NR/alive
[13]	Temporal	20/female	Temporal seizures	10 months	Transitional	1 year FU/NR/alive
[15]	–	8/male	–	–	Atypical	–
[8]	F-P	3/male	Seizures	2 years	Fibroblastic	7 years FU/NR/LFU
	Temporal	4/male	Sudden headache and altered mentality	1 day	Transitional	1 year FU/NR/alive
	Frontal	6/male	Headache, facial palsy, hemiparesis	2 weeks	Meningothelial	4 years FU/R/alive
	Temporal	9/male	Partial seizures	1 month	Sclerosing	13 months FU/NR/alive
	Frontal	19/male	Complex partial seizures	3 years	Fibroblastic	10 years FU/NR/alive
[12]	–	4/female	Temporal seizures	10 months	Fibroblastic	No recurrence
[7]	Frontal	33/female	Seizures	Not recorded	Transitional	Not recorded
Present study	Temporal	1.5/female	Generalised seizures	0.6 months	Transitional	4 years FU/NR/alive

None of the cases were associated with neurofibromatosis-2 (NF-2)

showing an isointense or hypointense mass on T1-weighted images, and a heterogenous mass surrounded by an area of increased intensity on T2-weighted images, the latter probably related to oedema or gliosis. Contrast-enhanced images generally vary from no enhancement to strong enhancement [9], causing difficulty in the presurgical evaluation of patients. In a study by Wiebe et al. [17], MRI in a few cases had suggested features mimicking low-grade tumours, vascular malformations and cystic encephalomalacia.

The diagnostic histological features of MA are leptomeningeal, meningothelial and meningovascular proliferation, which was seen in our case as well. Apart from this, the other features described in MA are degenerative calcification, gliosis, perivascular connective tissue proliferation, dysplastic neurons, white matter cysts, large-vessel hyalinisation, fibrocartilage formation and ossification [2]. When MA coexists with meningioma, the latter component is either transitional (56%), as seen in our case, or fibroblastic (31%) [8].Only a single case showed features of an atypical meningioma [8]. Most of the reported cases of MA with meningiomas showed brain invasion, although histologically they were composed of bland-looking cells without mitosis or necrosis [8]. Thus, the most vital differential diagnosis to be considered on histopathology is malignant meningioma [2, 11, 18], because infiltration of the cortex by the proliferating vascular cells, especially if associated with marked cellularity and reactive gliosis, may mimic a malignancy.

Overall, the pathogenesis of MA remains unclear. There are three main hypotheses [2, 11, 18]:

1. Hamartomatous lesion with degenerative change
2. Cortical vascular malformation that induces proliferation of cells from vessel walls or pluripotent arachidonic cap cells in the Virchow–Robin space
3. Direct invasion of the brain parenchyma by a leptomeningeal-based meningioma

The presumed hamartomatous or non-neoplastic theory is supported by their stability over a period of serial imaging, absence of appreciable proliferation in uncomplicated cases and lack of NF-2 mutations [18]. However, a recent report of an NF-2 gene deletion in one case of MA challenges this notion, raising the possibility that at least a subset of these may be neoplastic in origin [14]. This is further substantiated by a recent report by Sinkre et al. [15] on a case of atypical meningioma juxtaposed with MA. Regardless of the pathology, MA is a slow-growing lesion, demonstrating low MIB-1 labelling index [11]. It has been reported that chronic leptomeningeal stimulation by an underlying cortical lesion could also result in MA-like histopathological changes [2].

Partial or complete resection has been advocated for prompt seizure control in cases of MA [1]. However, studies [2] have reported that despite adequate surgical resection of the lesion, seizures persisted in a significant number of cases, and in more than 70% of the patients antiepileptic drugs had to be continued, even several years after removal of MA [2]. In contrast, cases of MA with meningioma had a more favourable outcome after surgical resection. In the 11 cases for which follow-up studies are available, only one case had recurrence, necessitating second surgery [1, 3, 4, 8, 12, 13]. In our patient, a follow-up of 40 months is available, during which she has remained seizure free.

Meningiomas in paediatric patients are a rarity, comprising approximately 1 to 3.5% of all intracranial tumours [8], and associated with more aggressive clinical behaviour and a higher rate of malignant transformation than their adult counterparts. Thus, MA coexisting with meningioma in the paediatric age group, like our case, should be evaluated with adequate caution [19] for features of atypia (like mitoses, necrosis and sheeting), and brain invasion, which are the traditional determinants of malignant meningioma.

In conclusion, MA is a benign and possibly hamartomatous lesion of childhood typically presenting with seizures, and uncommonly associated with an underlying meningioma. Surgery is the recommended therapy, given the excellent outcome even after partial excision of the lesion. Recognition of these rare coexistent conditions is vital, to avoid unnecessary postoperative radiation or additional treatments due to erroneous interpretation as aggressive meningiomas.

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