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Case Report

B-cell central nervous system lymphoma developing in a patient with cerebral meningioangiomatosis

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ABSTRACT

Meningioangiomatosis is a rare congenital hamartomatous malformation of the leptomeninges that can also involve the adjacent cerebral tissue, sometime arising in association with neurofibromatosis. Here we report the case of a 55-year-old man with neuroradiological evidence of meningioangiomatosis, known to be a well-defined malformative-dysplastic lesion, preceding the onset of central nervous system B-cell lymphoma. We describe for the first time this unusual association, highlighting how meningioangiomatosis could accompany different pathologies more frequently than thought.

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Introduction

Meningioangiomatosis is an uncommon benign hamartomatous proliferation of the leptomeninges. Initially described in association with neurofibromatosis (NF) by Worcester-Drought et al [1], at present it is known to arise also sporadically, in absence of other type of lesions. Meningioangiomatosis arises from cerebral cortex and leptomeninges, and it is characterized by abnormal meningo-vascular proliferation and leptomeningeal calcification [2]. We report the case of a patient with history of meningioangiomatosis who developed

a large B cell central nervous system (CNS) lymphoma few years after the initial diagnosis.

Case report

A 55-year-old man with congenital cognitive impairment referred to the emergency unit for a first episode of epilepsy with generalized seizures. Anamnestic data collection revealed sporadic episodes of altered conscious state and gestural automatism within previous months, sometimes preceded

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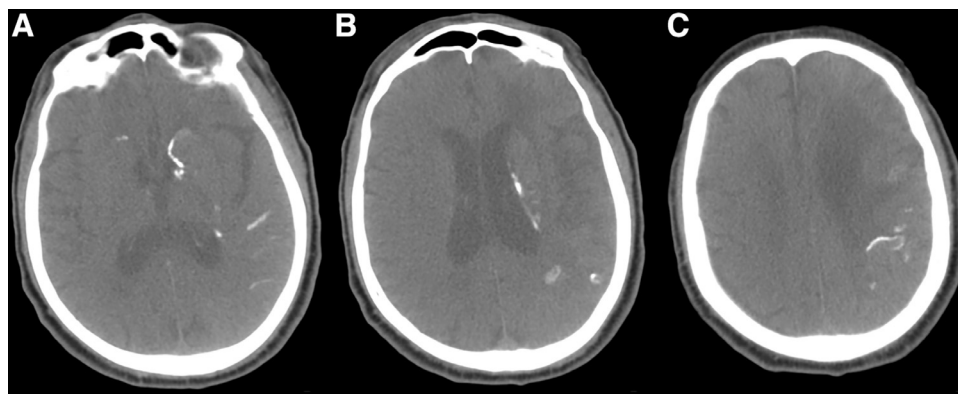


Fig. 1 – Prelymphoma onset CT examination, performed at the age of 55-year old. Axial brain CT slices (bone window) at three representative levels (A-C).

by paraesthesia of the upper right limb. A brain computed tomography (CT) scan performed at the admission to hospital revealed a large left temporo-parietal and nucleo-capsular expansive lesion with some meningeal and/or cortical calcifications combined with some scattered thin calcifications located in deep brain structures. Some calcifications were also noted superficially to the superior right frontal gyrus in the right nucleocapsular region and in the left dentate nucleus (Fig. 1). A subsequent contrast-enhanced magnetic resonance imaging (MRI) confirmed a diffuse alteration of the left hemispheric white matter extending to the trigone and the adjacent periventricular region and capsule system; streaks of TSE T2w and GRE T2w hypointensity were present in the left parietal region, head of the caudate nucleus, putamen and thalamus, probably due to calcium or hemosiderin deposition. After intravenous contrast agent administration, diffuse postcontrast leptomeningeal enhancement was visible within the left temporal-parietal-occipital cortex, nucleo-capsular, and peritrigonal regions, along with gyral enhancement of the right superior frontal sulcus (Fig. 2). The patient was subsequently transferred to the department of neurology for further clinical examinations. The neuropsychological evaluation revealed alterations in attentive-executive functions with a slight memory and verbal impairment. These findings suggested the diagnosis of meningioangiomatosis confirmed by biopsy (not shown). The patient was therefore discharged with the final diagnosis of drug-resistant symptomatic focal epilepsy related to meningioangiomatosis, and an adequate clinical and radiological follow-up was scheduled.

During the follow-up over the following years, the patient showed a progressive cognitive deterioration with walking limitations, mixed aphasia, depressive behavior, reduced verbal fluency, and memory. After 8 years, at follow-up neurological examination, the patient presented with severe deterioration of consciousness (aroused only by verbal stimulation), mixed aphasia (with dominant fluency impairment), right facial-brachial-crural hemiplegia with inability to stand, walk, or even sit without assistance. Therefore, the patient underwent a new contrast-enhanced MRI examination. The MRI confirmed an increase in volume of the left parieto-

occipital lesion, spreading into the splenium of the corpus callosum and the ventricular ependymal layer, showing intense water restriction on diffusion weighted imaging (DWI) and homogeneous enhancement after contrast media administration. The adjacent ventricular and cysternal structures were compressed with contralateral shift of the midline structures and subfalcine herniation of the left cingulate gyrus and uncus herniation compressing the left cerebral peduncle (Fig. 3).

The patient underwent surgery with partial excision of the expansive lesion through a left parietal craniotomy. The histological examination showed brain tissue infiltrated by a hypercellulated neoplasia consisting of large lymphoid elements, strongly positive to CD20. These findings were consistent with the new diagnosis of a large B cell CNS lymphoma (Fig. 4).

Discussion

Meningioangiomatosis is a rare benign proliferative lesion, which usually affects meningotheelial cells, leptomeningeal vessels, and the underlying cerebral cortex, sporadically involving the thalamus and the brainstem [3,4]. Many cases have been reported in association with neurofibromatosis type 2 (NF2), Sturge-Weber disease, and other phakomatosis, as well as other rare conditions [5–8].

With a slightly higher prevalence in males and young adults [9,10] from a clinical point of view meningioangiomatosis usually characterized by headaches and drug-resistant seizures. Several cases have also been described as incidental findings at imaging examinations or autopsy, especially in elderly subjects and in NF2 patients.

Meningioangiomatosis usually affects the frontal and temporal brain cortex, but can also involve other deep structures such as the thalamus, the third ventricle, and the brainstem [2,11], as in the present case.

The pathogenesis of meningioangiomatosis is still largely unknown, but it is generally considered a condition of hamartomatous origin [12]. In patients with NF2, the cause can be attributed to focal areas of hyperplasia or dysplasia within the arachnoid, whereas in other patients the pathogenesis is

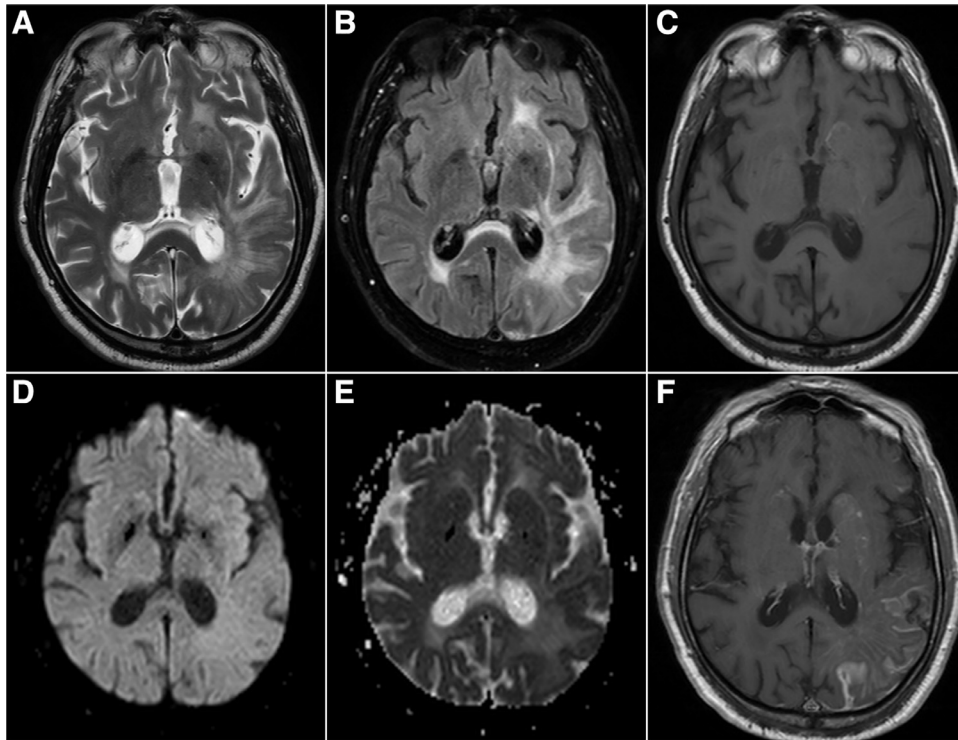


Fig. 2 – Prelymphoma onset MRI examination, performed at the age of 55-year old. Axial TSE T2W (A); axial FLAIR T2w (B); axial SE T1w (C); axial DWI (D) with relative ADC map (E); postcontrast axial SE T1w (F).

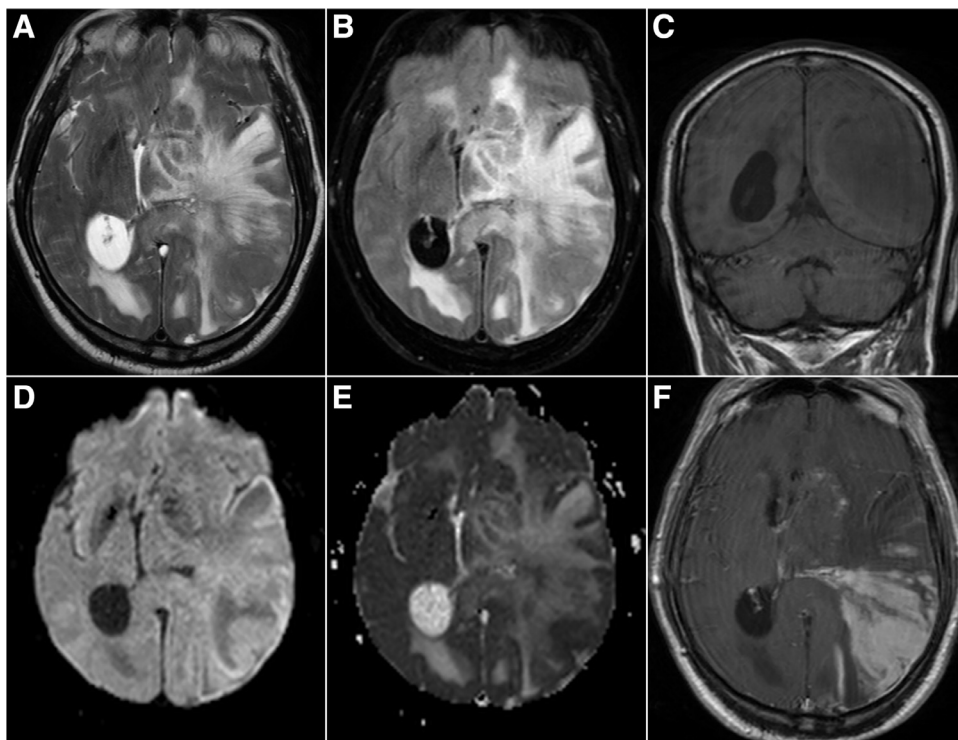


Fig. 3 – Postlymphoma onset MRI examination, performed at the age of 63-year old. Axial TSE T2W (A); axial FLAIR T2w (B); coronal SE T1w (C); axial DWI (D) with relative ADC map (E); postcontrast axial SE T1w (F).

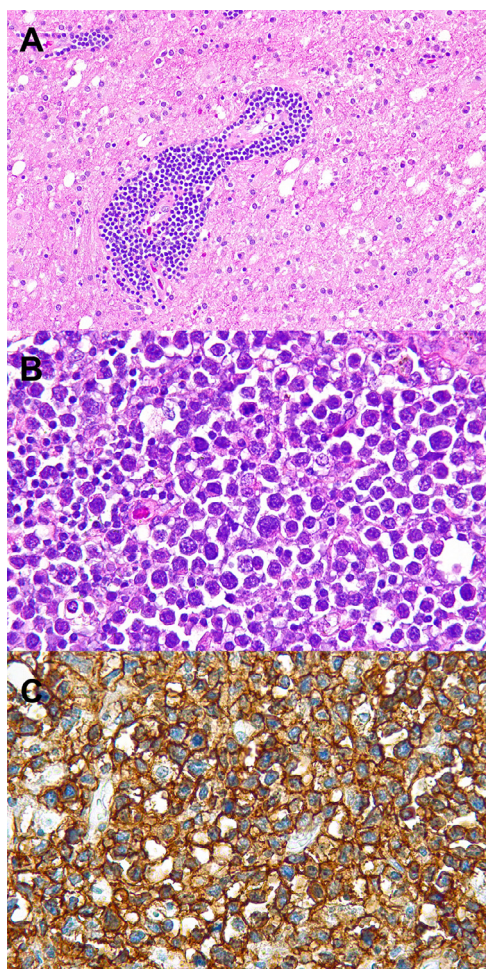


Fig. 4 – Pathologic examination of surgical specimen. **At the periphery, neoplastic cells are arranged around vessels, forming perivascular cuffs (A – H&E, 20x magnification). The lymphoproliferative neoplasm is composed by large atypical cells with large round, oval, irregular or pleomorphic nuclei and indistinct nucleoli (B – H&E, 40x magnification). Immunohistochemistry shows strong positivity to CD20 in neoplastic cells (C – 40x magnification).**

more debated. The 3 most reliable hypotheses on meningoangiomas pathogenic mechanism are [13]:

- congenital hamartomatous development;
- direct invasion of brain tissue from a leptomeningeal meningioma;
- initial development of angiomatous tissue with meningoangiomas components arising secondarily from the perivascular elements.

Concerning pathologic evaluation, the lesion could simulate a schwannoma due to some common characteristics such as basal lamina, palisading arrangement of tumor cells, wavy nuclei, and positive staining for S100 protein; on the other hand, differential diagnosis suggestive features consist of perivascular arrangement of the cells and marked calcifica-

tion besides focal immunohistochemical staining for smooth muscle actin (SMA) [13].

Calcifications (either linear or granular) are the most pictorial finding on CT examination, while noncalcified areas could be isodense to hypodense [11]. At MRI the lesions are isointense to hypointense to gray matter on T1w sequences and hyperintense to hypointense on T2w sequences. Some hypointense areas due to susceptibility artifacts on T2* images and susceptibility imaging are frequently observed, related to calcifications (89.6%); sometimes a simultaneous vasogenic edema in the adjacent brain tissue has also been described [3,4]. Various types of enhancement patterns have been reported, ranging from absent to intense and homogeneous enhancement, this latter considered the most common with an estimated prevalence of 79.6% [14].

Due to its pleomorphic CT/MRI appearance and variable location (either intra- or extra-axial), meningoangiomas diagnostic assessment can be particularly challenging, often requiring the exclusion of possible mimickers and the biopsy confirmation. Meningoangiomas differential diagnoses include artero-venous malformation, meningiomas, gliomas, oligodendrogliomas, and granulomatous meningitis (such as tuberculosis or sarcoidosis) [15,16]. A gyriform hyperintensity on T2w sequences has been reported as the most prominent characteristic for sporadic meningoangiomas, while multifocal cerebral localizations have also sporadically been reported; a possible role of new advanced MRI techniques in detecting meningoangiomas typical features should however further be investigated [17–22].

It is well known that meningoangiomas represents a typical finding in phakomatoses such as Sturge-Weber syndrome, sometimes representing the only initial manifestation of the disease without other syndrome's stigmata. For this reason, in case of meningoangiomas it is important to investigate the spectrum of Sturge-Weber manifestations, in order to exclude a type 3 syndrome according to Roach [23]. More inconstant associations include vascular disorders, such as cerebral hemorrhage and arteriovenous malformations [24].

Meningioma is the most commonly associated neoplasm, while other possible codiagnoses also include oligodendroglioma and meningeal hemangiopericytoma; the mechanisms underlying this association is unknown, but chronic leptomeningeal stimulation resulting in histopathological changes of adjacent brain and meningeal tissue is one of the most accepted hypotheses [24]. At present, this is the first report of meningoangiomas and large B cell CNS lymphoma in the same patient, not allowing assessing whether this could be considered as a codiagnosis or a random coexistence. However, it must be noticed that the incidence of CNS neoplasm such as meningiomas and lymphomas in patients with phakomatoses (the most common complex disorder associated to meningoangiomas) is higher compared to the general population [25], suggesting a possible link between these two conditions. In this light, a larger data collection is warranted to clarify the mechanisms underlying this unusual finding.

In conclusion, the association between meningoangiomas and lymphoma has never been described in current scientific literature. This case report highlights the importance of an accurate analysis of imaging studies performed

over time in order to track the evolution of the disease, suggesting a possible role of advanced MRI techniques in the correct diagnostic assessment. We also highlight that meningioangiomas could accompany different pathologies more frequently than thought, proposing further connections with various lymphoproliferative disorders.

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Conflict of interest

The Authors declare that there is no conflict of interests regarding the publication of this paper. The Authors alone are responsible for the content and writing of the paper.

Ethical approval

All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent

Informed consent was obtained from all individual participants included in the study.

Authors contribution

All authors make substantial contributions to conception and design, and/or acquisition of data, and/or analysis and interpretation of data according to ICMJE recommendations. All those who have made substantive contributions to the article have been named as authors.

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