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EC NEUROLOGY
Case Report

Early-Onset Dementia, Seizures and Thick T2-Hyperintense Cortex due to Low Grade, Small B-Cell Lymphoma. A Case Report

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Abstract

A 57-year-old man presented with dementia and recurrent status epilepticus. Neuroimaging revealed bilateral cortical thickening, evident in CT scan and MRI, with hyperintensity on T2-weighted sequences but without enhancement after gadolinium. Analysis of cerebrospinal fluid as well as total body CT scan and laboratory exams were unremarkable. A brain biopsy of right frontal lobe cortex was performed. Overall, the findings were compatible with low malignant primary central nervous system (PCNS) lymphoma, presumably follicular or marginal zone subtype. The patient reported here has very unusual neuroimaging findings, as well as some atypical clinical features for PCNS lymphoma: long disease course, absence of focal neurological signs. Low-grade CNS lymphoma should be suspected in the differential diagnosis of patients with early-onset dementia and seizures. Brain biopsy is the diagnostic gold standard.

Keywords: *CNS Lymphoma; Status Epilepticus; Low-Grade; Early-Onset Dementia; Histopathology*

Abbreviations

PCNS: Primary Central Nervous System Lymphoma; MRI: Magnetic Resonance Imaging; FLAIR: Fluid Attenuated Inversion Recovery; CSF: Cerebrospinal Fluid; NMDA-R: N-Methyl-D-Aspartate Receptors; GABA: Gamma-Amino-Butyric Acid; VGKC: Voltage-Gated Potassium Channels; AMPA: Ammino-3-Idrossi-5-Metil-4-Isossazol-Propionic Acid; MOG: Myelin Oligodendrocyte Glycoprotein; AQP4: Aquaporin-4; GAD: Glutamic Acid Decarboxylase

Introduction

A clinical picture characterized by progressive cognitive decline and epileptic seizures in a previously healthy adult may recognize many differential diagnoses, including neurodegenerative, inflammatory, infectious and neoplastic diseases. Primary central nervous system (PCNS) lymphoma represents an uncommon subtype of extranodal lymphoma involving the brain, leptomeninges, eyes, or spinal cord without systemic localizations. It represents less than 5% of PCNS tumors, with an incidence rate of 4/1,000,000/year [1,2]. In most

cases, PCNS lymphomas are of B cell phenotypic origin; more than 80 per cent are aggressive or highly aggressive, diffuse large cell lymphomas [3,4]. Hodgkin type and low-grade PCNS lymphomas are exceedingly rare [5,6]. The latter has a better long-term outcome than aggressive histology PCNS lymphoma [5]. PCNS lymphoma usually presents at magnetic resonance imaging (MRI) as single or multifocal brain lesions, often involving periventricular areas, with a strong and uniform signal enhancement after gadolinium.

Case Report

Herein, we describe a 57-year-old man presenting with a 3-year history of progressive cognitive impairment and recurrent episodes of focal onset evolving into bilateral convulsive status epilepticus. Upon examination, the patient was alert, oriented in space and non-oriented in time, without focal neurological signs. Neuropsychological evaluation revealed an impairment in frontal functions. Brain CT scan (Figure 1A) showed thickening with hyperdensity of fronto-parieto-temporal cortices bilaterally. MRI (Figure 1B and 1C) disclosed hyperintensities of fronto-temporo-parietal cortices bilaterally in T2-FLAIR sequences, without gadolinium enhancement. Serum and CSF search for anti-NMDA-R, anti-GABA, anti-VGKC, anti AMPA-R, anti-MOG, anti-AQP4, anti-GAD and anti-neuronal antibodies, screening for neurotropic viruses and HIV were negative. Lymphocytes subpopulation in peripheral blood showed increased CD4/CD8 ratio. A brain biopsy of right frontal lobe cortex (Figure 2A) showed dense mononuclear infiltrates of lymphocytes with small and monomorphic shape, without lymphoid blasts. At immunohistochemistry, CD20-positive B lymphocytes co-expressing Bcl-2 were identified (Figure 2B). No expression of CD23, Cyclin D, CD5 and CD25 was noted. Further molecular pathology analyses revealed a monoclonal rearrangement pattern in the variable region of the heavy immunoglobulin chain with primers Fr2A, LJH and VLJH (Figure 2C). Overall, the findings were compatible with a low malignant PCNS lymphoma, presumably follicular or marginal zone subtype.

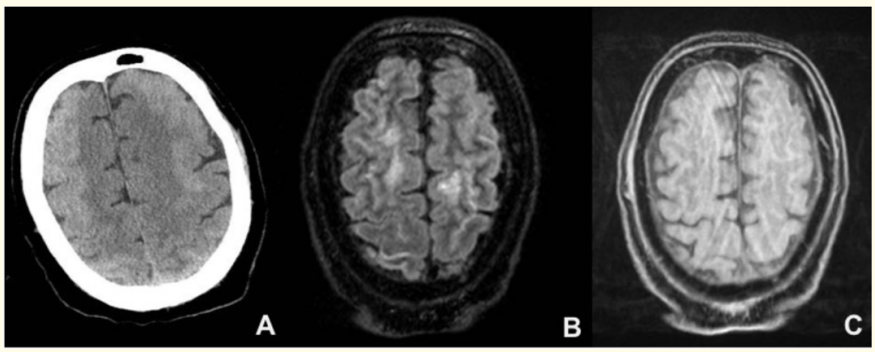

Figure 1: *Neuroimaging. Figure 1A: CT scan. Figure 2B: MRI, axial FLAIR sequence. Figure 2C: MRI, post-gadolinium axial T1 sequence.*

Discussion

The patient reported here has some atypical features for PCNS lymphoma: a long disease course, the absence of focal neurological signs, unusual neuroimaging findings (MRI T2-hyperintense/CT-hyperdense cortices, absence of contrast enhancement). The largest reported case series of low-grade primary CNS lymphoma [2] identified 40 patients in 18 cancer centers from 5 countries. Clinical and MRI features were different from those of high-grade PCNS lymphomas. In particular, a milder clinical course and a longer survival were observed; unusual MRI features included hyperintensity on T2-weighted images (40%), inhomogeneous or moderate contrast enhancement (56%), lack of periventricular localization (24%) [2]. A single patient showed no contrast enhancement in this series. Similar MRI

features were noted in another case series comprising ten patients with low grade PCNS lymphoma [3]. Brain biopsy represents the gold standard for the diagnosis of PCNS lymphoma, a rare but potentially treatable disorder which should be considered in the differential diagnosis of patients presenting with progressive neurological signs, neuropsychiatric symptoms, seizures and MRI T2-hyperintense/CT-hyperdense brain lesions.

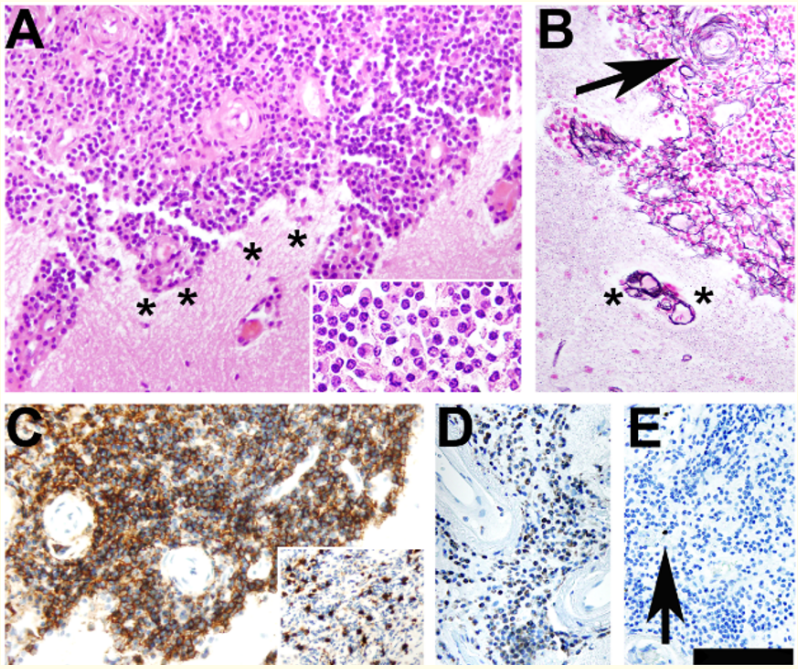

Figure 1: *Neuropathology. Figure 2A: Hematoxylin and eosin staining, bar graph corresponding to 100 µm; insert: bar graph corresponding to 30 µm. Figure 2B: Hematoxylin and eosin staining, bar graph corresponding to 100 µm. Black arrow, physiologically shaped vessel marked by asterisks for comparison. Figure 2C: immunohistochemistry for CD3 and CD20, bar graph corresponding to 100 µm; insert: bar graph corresponding to 100 µm. Figure 2D: immunohistochemistry for Bcl-2, bar graph corresponding to 100 µm. Figure 2E: immunohistochemistry for Ki67, bar graph corresponding to 50 µm.*

Conclusion

We present a rare case of low-grade primary CNS lymphoma, whose imaging features were inconclusive.

Pathological data were indispensable to reach correct diagnosis.

Conflict of Interest

None.

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