Seizure 22 (2013) 901–904

Contents lists available at ScienceDirect

Seizure

journal homepage: www.elsevier.com/locate/yseiz

Short communication

Pathology of bilateral pulvinar degeneration following long duration status epilepticus

Aurelio Hernandez-Lain [a,d], E. Tessa Hedley-Whyte [a], Lida P. Hariri [a], Bradley Molyneaux [b,c], Keith J. Nagle [e], Andrew J. Cole [b,c], Ronan Kilbride [b,c,*]

[a] Charles S Kubik Laboratory for Neuropathology, Department of Pathology, Boston, MA, USA
[b] The MGH Epilepsy Service, Department of Neurology, Massachusetts General Hospital , Boston, MA, USA
[c] Departments of Pathology and Neurology, Harvard University, Boston, MA, USA
[d] Servicio de Anatomía Patológica (Neuropatología) and Instituto de Investigación i+12, Hospital Universitario 12 de Octubre, Madrid, Spain
[e] Department of Neurology, University of Vermont College of Medicine, Burlington, VT, USA

ARTICLE INFO

Article history:
Received 7 March 2013
Received in revised form 16 July 2013
Accepted 17 July 2013

Keywords:
Status epilepticus
Epilepsy monitoring
MRI
Spinal cord
Medical/systemic disease

ABSTRACT

Purpose: To define the neuropathological findings of pulvinar degeneration seen in long duration status epilepticus.
Methods: We review the clinical, radiologic, neurophysiologic, investigational and neuropathological findings on a 27 year old woman who died after 162 days of prolonged refractory status epilepticus.
Results: Continuous EEG monitoring confirmed recurrent uncontrolled seizure activity bilaterally and independently, most frequent in the right fronto-temporal region. Initial MRI of the brain was normal. Repeat study until on day 127 of admission showed advanced changes, with bilateral pulvinar T2/FLAIR hyperintensities. The autopsy revealed sharply defined, grey, soft, granular nodules in each medial pulvinar nucleus. Microscopically these consisted of sharply defined paucicellular areas with loss of neurons and myelin and with numerous macrophages in their centers, surrounded by reactive astrocytes with relatively spared of axons. The spinal cord at cervical and thoracic levels showed symmetric spongy vacuolation in the central part of the dorsal columns and lateral corticospinal tracts, with mild myelin loss, relatively preserved axons. The pathological lesions found in this case in thepulvinar are somewhat similar to the pathologic lesions described in Wernicke's encephalopathy. Those found in the spinal cord of our patient resemble characteristic features of B12 related subacute combined degeneration.
Conclusion: Characteristic pulvinar degeneration may be found as an acquired phenomenon in prolonged refractory status epilepticus. We hypothesize that the neuropathological findings result from an excessive focal metabolic demand, secondary to neuronal network over activation in the setting of prolonged, frequent bi-temporal seizures.

1. Introduction

Acquired neuroimaging changes of the pulvinar nuclei is a known MRI finding in patients with refractory seizures.[2,4] However, only one autopsy study of a patient with new onset refractory status epilepticus with pulvinar lesions in diffusion MRI has been reported.[1] We report the neuropathological changes in a case with characteristic neuroimaging secondary to prolonged refractory status epilepticus (PRSE) with associated new and novel thalamic and spinal cord pathology.

2. Clinical data

27 year old woman with past history of two neonatal febrile seizures, admitted to hospital because of the acute onset of confusion and increasing somnolence, preceded by 5 days of flu-like symptoms and low grade fever. On hospital day 2 she

* Corresponding author at: Department of Neurology, Massachusetts General Hospital, 55 Fruit Street, WAC 835, Boston, MA 02114, USA/Servicio de Anatomía Patológica (Neuropatología) and Instituto de Investigación i+12, Hospital Universitario 12 de Octubre, Madrid, Spain.
E-mail addresses: ahernandez.hdoc@salud.madrid.org (A. Hernandez-Lain), rkilbride@partners.org (R. Kilbride).

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http://dx.doi.org/10.1016/j.seizure.2013.07.012

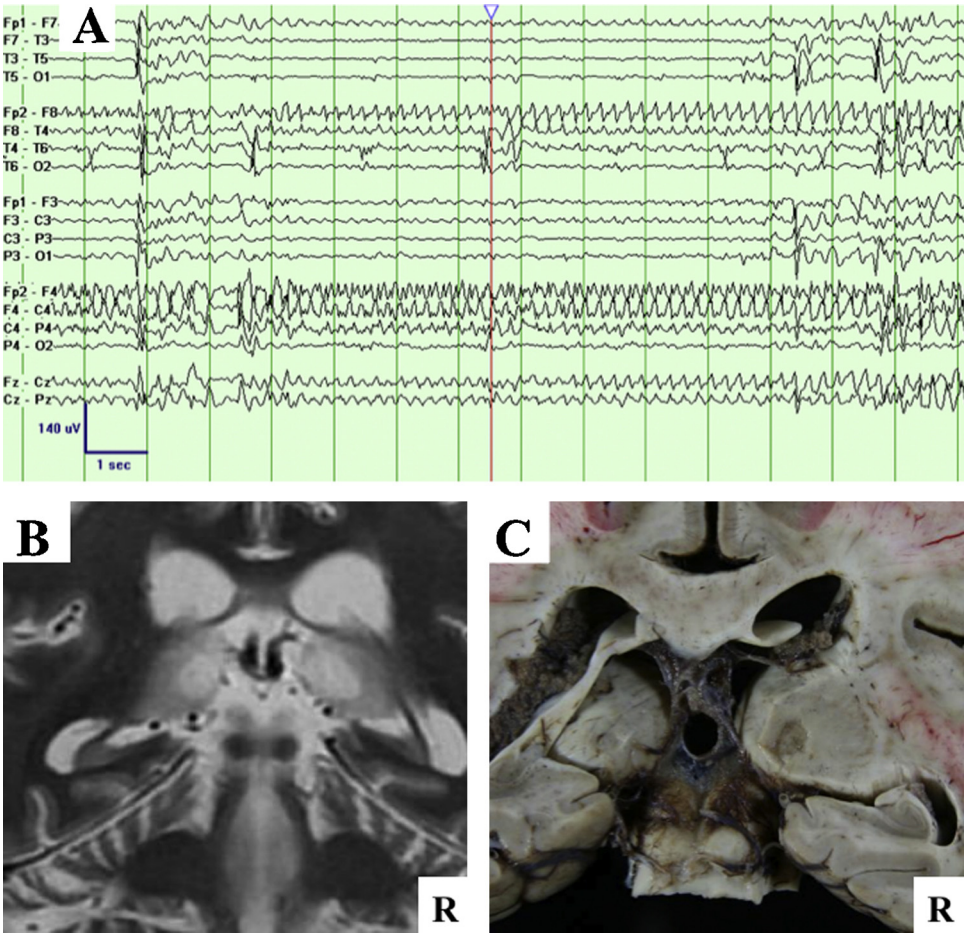

Fig. 1. EEG on day 152 (10 days prior death), showing the right fronto-temporal seizure and independent left temporal sharp waves. (A) Coronal T2 MRI on day 127 at the level of the superior colliculi showing increased signal in both pulvinar nuclei. (B) Coronal sections of the formalin-fixed brain at the corresponding level to A. Note the sharply defined, sunken yellow-gray area in each pulvinar nucleus. The right hippocampus is smaller than the left and the right temporal horn is larger that the left in both B and C. Note the MRI has been reversed so that in both pictures the right hemisphere is on the right (C) (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.).

sustained 2 generalized tonic-clonic seizures followed by recurrent medication refractory status epilepticus. Continuous EEG monitoring throughout her illness confirmed recurrent uncontrolled seizure activity bilaterally and independently over both hemispheres but notably most frequent in the right fronto-temporal region (Fig. 1A). These seizures remained refractory to maximal anti-epileptic drug and anesthetic therapies. Despite extensive medical evaluation, including multiple CSF and serum tests and a normal brain biopsy performed on day 14, the cause for the refractory status epilepticus remained cryptogenic. Serum folate and B12 levels on day 84 were normal. Multiple neuroimaging studies (MRI) of the brain were normal until day 127 when an MRI showed new bilateral pulvinar DWI/T2/FLAIR hyperintensities and selective right mesial temporal atrophy (Fig. 1B). In spite of aggressive medical treatment and support, seizures remained uncontrolled, the patient developed renal and cardiac failure, and died on hospital day 162. An autopsy was performed.

3. Pathological findings

The brain weighed 1340 g. The right hippocampus was smaller than the left. A sharply defined, gray, soft, granular nodule was present in each medial pulvinar nucleus, 1.3 cm greatest diameter on the right and 0.7 cm on the left (Fig. 1C).

The nodular lesions in the pulvinar nuclei consisted of sharply defined paucicellular areas with loss of neurons and myelin and with numerous foamy lipid-laden cells in their centers (Fig. 2A), surrounded by reactive astrocytes (Fig. 2B), CD-68 immunostains confirmed that most of the foamy cells were macrophages (Fig. 2C). Neurofilament antibody revealed relatively spared axons within the lesion but with a distorted morphology. The mid thalamus and the periaqueductal gray matter revealed reactive astrocytes and proliferative small blood vessels but no loss of neurons. No abnormalities were found in the mammillary bodies. The right hippocampus showed severe neuronal loss, many reactive astrocytes and capillaries with prominent endothelial cells, particularly in CA1 and to a lesser extent in the subiculum, CA2, CA3 and CA4 consistent with subacute damage (Fig. 2D). The spinal cord at cervical and thoracic levels showed symmetric spongy vacuolation in the central part of the dorsal columns and lateral corticospinal tracts, with mild myelin loss, relatively preserved axons (Fig. 2E). CD-68 immunostains confirmed the presence of macrophages in the spinal tracts with vacuolar changes (Fig. 2F).