Post-Encephalitic Parkinsonism and Sleep Disorder Responsive to Immunological Treatment: A Case Report

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Introduction: Post-encephalitic parkinsonism (PEP) has an immune-mediated pathogenesis. PEP was associated with encephalitis lethargica, also known as von Economo disease.

Case report: An elderly man developed fever and a neurological syndrome consistent with an encephalitis of undetermined etiology, likely viral. He rapidly recovered but successively, within 2 to 4 weeks from the onset, he presented a neurological disorder, characterized by lethargy and parkinsonism, suggestive of encephalitis lethargica—PEP.
EEG recordings showed different pattern: during wake, bilateral, reactive alpha activity was present (Figure 1A). During lethargic periods theta activity predominated on the posterior areas, whereas alpha was predominantly anterior; sporadic vertex spikes were observed (Figure 1B). During sleep, NREM and REM sleep patterns were observed (Figure 1C).
Polysomnographic monitoring was consistent with a severe disruption of sleep: the sleep-wake cycle was fragmented, and the NREM-REM ultradian cycle was irregular (Figure 2A).
Brain MRI performed at day 15 showed hyperintense signal in T2-weighted imaging in the hippocampi and in the thalami bilaterally (Figure 3B).
Patient's serum and CSF were tested for IgG specific to GAD65 and onconeural, synaptic or unclassified antigens by indirect immunofluorescence on frozen sections of mouse brain and by cell-based assays. IgG from the patient's serum bound to the neuropil of mouse brainstem, in particular in the mesencephalon, suggesting the presence of IgG specific for an unclassified neuronal antigen (Figure 3C).
Therefore, immunologic treatment with Igiv was started resulting, within 7 days, in an improvement of motor performance, reduction of lethargy and amelioration of the sleep-wake behavior. MRI performed at day 30 was normal (Figure 3B).
A follow-up evaluation was performed 2 months later: the patient had fully recovered and PSG demonstrated a substantially normal sleep-wake pattern (Figure 2C).

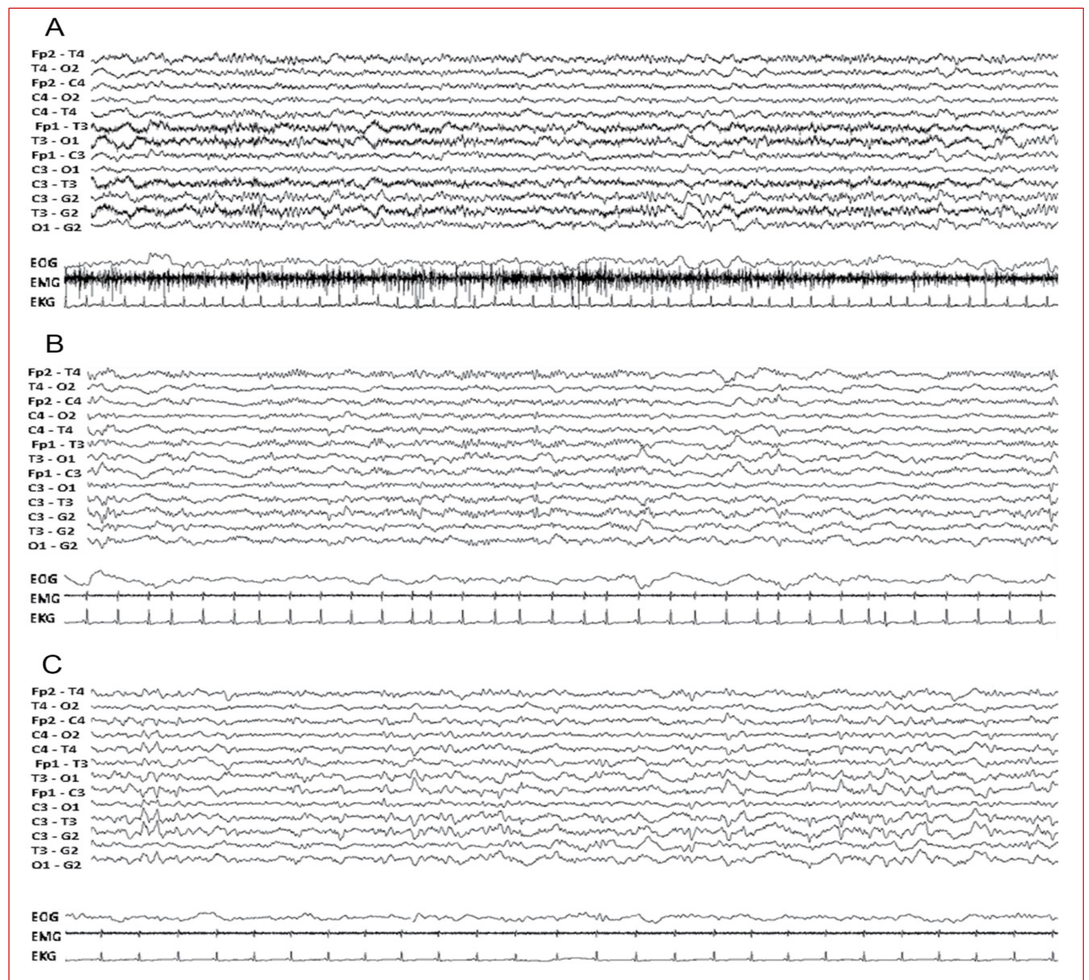

Figure 1. Electroencephalography (EEG) recording patterns during wake (A), lethargic periods (B) and sleep (C).

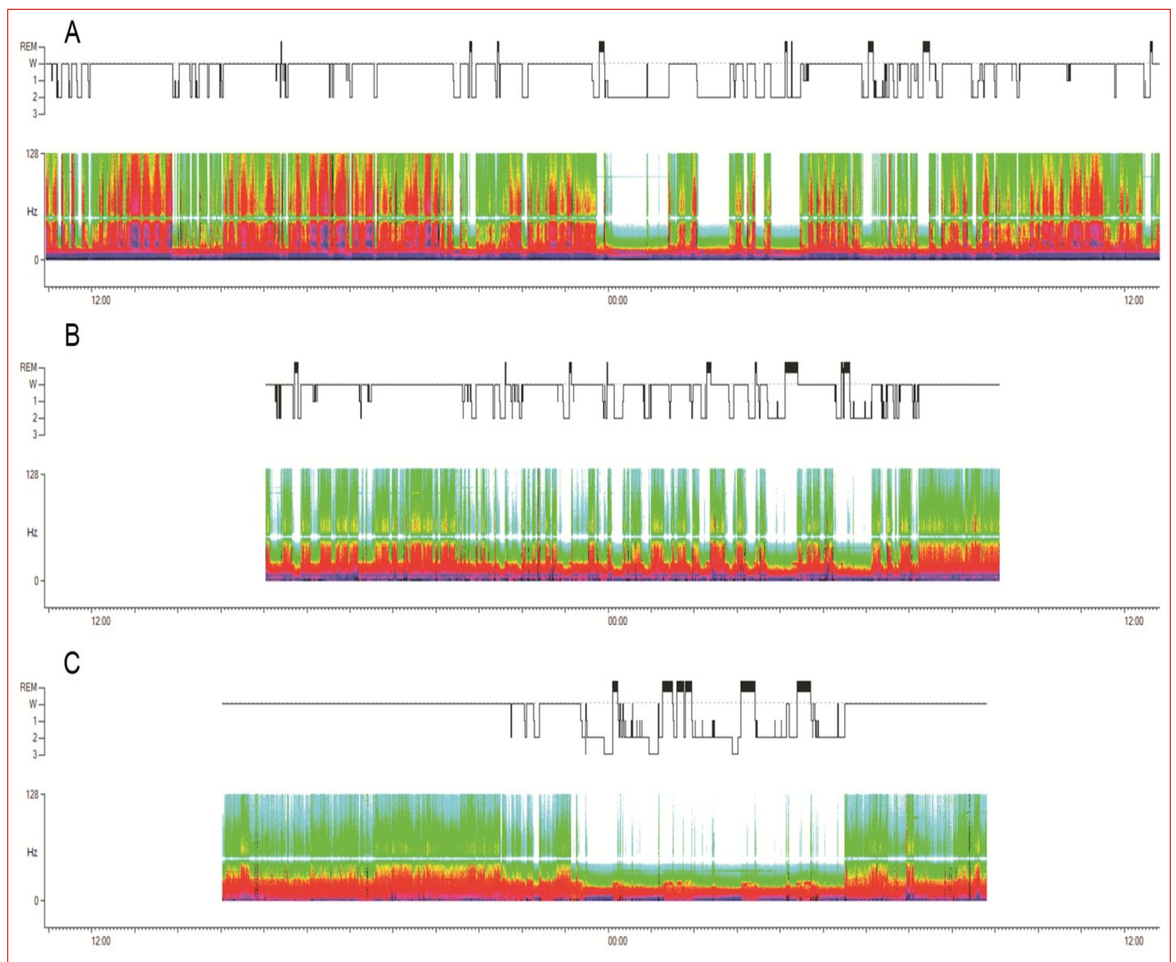

Figure 2. Sleep hypnograms obtained at day 15 (A), at day 30 (B) and at day 60 (c).

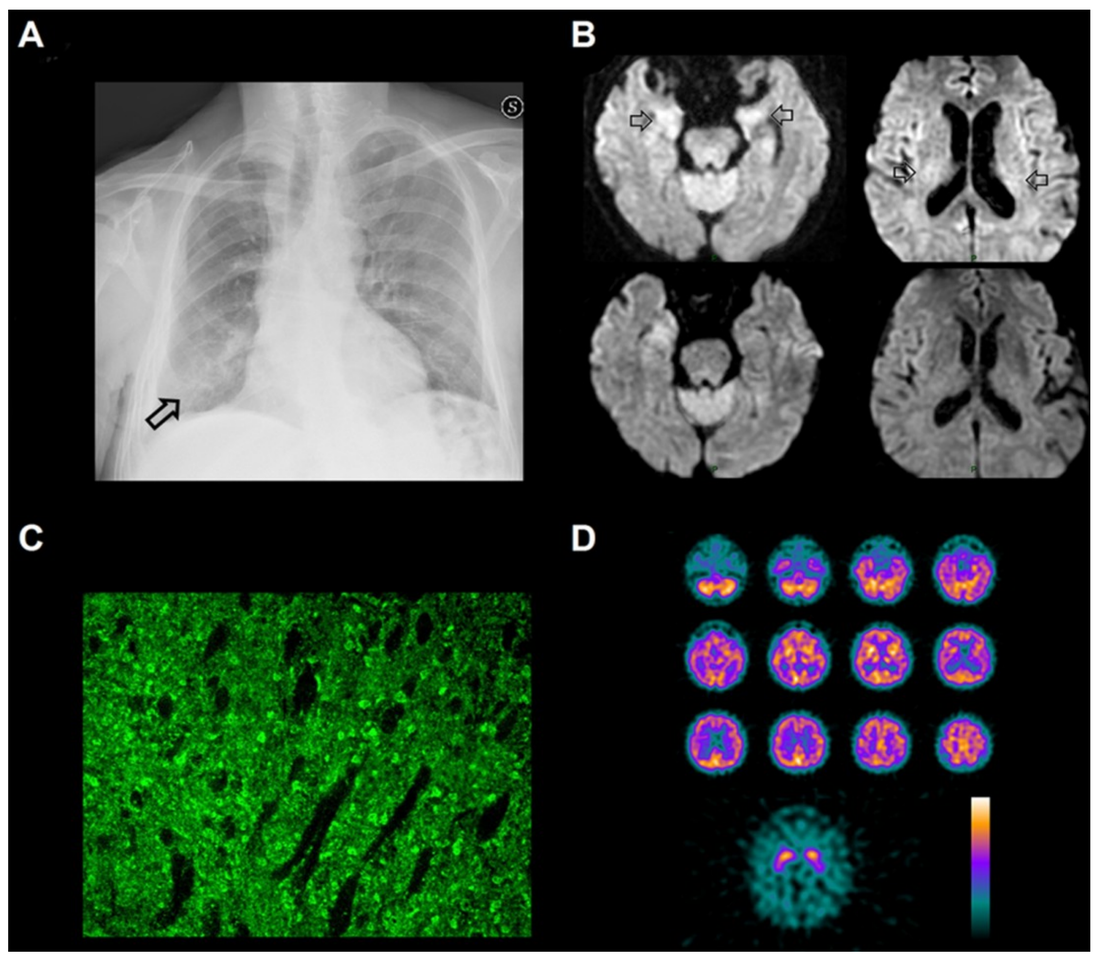

Figure 3. Multimodal imaging of the post-encephalitic parkinsonism. (A) Chest radiograph; a focal area of pulmonary parenchymal consolidation is visible in the lower right lobe (arrow). (B) Magnetic resonance diffusion-weighted imaging (MR-DWI), in axial plane, performed at day 15 (upper panel) and at day 30 (lower panel). (C) Immunohistochemistry (indirect immunofluorescence assay on mouse midbrain): IgG in patient's serum (1:200) binds to the midbrain neuropil. Magnification 10×. (D) Upper panel: Transaxial 99mTc-HMPAO SPECT slices (1 pixel thick), showing a nonhomogeneous radiotracer uptake in the left frontoparietal cortex as well as small areas of reduced uptake in the pons, left temporal cortex (anteromesial region) and left cerebellar hemisphere. Lower panel: Transaxial ^{123}I-FP-CIT SPECT slice at the level of the striatum. A slight and relatively asymmetrical reduction in radiotracer uptake can be observed in the putamina (left < right), whereas activity is still regular in the caudate nuclei.

Discussion: In our case, the delay between the resolution of encephalitis and the onset of the movement and the sleep disorder suggest that this syndrome may be considered post-encephalitic; the immunohistochemical analysis and the prompt response of the symptoms to Igiv support an immune-mediated pathogenesis. Our hypothesis is that parkisonism and sleep modifications are the expression of an immune-mediated attack of structures in the brainstem. Dysfunction of the ponto-mesencephalic reticular formation may impair arousal reaction, inducing inability to keep the awake state.

Conclusions: Parkinsonism and sleep disorders may be consequences of encephalitis, an immune-mediated pathogenesis is likely, and, consequently, immunotherapy can be beneficial. The polysomnographic monitoring suggests that lethargy, rather than a mere hypersomnia, is the result of a combination of sleep disruption and altered motor control.

Reference:
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