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Progressive mental status changes and seizures with FLAIR hyperintensity on brain MRI

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Keywords

Antibody; limbic encephalitis; N-methyl-D-aspartate receptor; paraneoplastic

1. Clinical background

A 31-year-old male presented to the hospital with disorientation and leg weakness after running. Several weeks prior to admission, he developed visual changes, described as yellow plastic masks of peoples' faces. Over the past week, he complained of headaches, right foot numbness, and intermittent loss of leg control when running. At times, he developed spontaneous extension of the right leg and inversion of the foot, tremulousness, and weakness lasting several seconds. Neurological exam was notable for impaired mental status with disorientation to date and place. Mood was labile with behavioral outbursts. He had marked abulia and mild anomia. Memory was poor with inability to recall daily and past details. His motor exam was notable for increased tone and clonus in his lower extremities. While in the hospital, he had periods of hypertension and tachycardia.

2. What is the most likely diagnosis?

A. Anterior cerebral artery stroke

B. NMDA receptor autoimmune encephalitis

C. Intravascular lymphoma

D. Creutzfeldt-Jakob disease

1. Answer

B) NMDA receptor autoimmune encephalitis

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2. Discussion

Both serum and cerebrospinal fluid from this patient contained IgG that bound to CNS tissues in a pattern consistent with NMDA receptor specific-IgG (Figure 2A and B; immunofluorescence titer [expressed as the reciprocal of doubling serum dilutions] was 3840). NMDA receptor specificity was confirmed using NMDA receptor transfected and nontransfected cells (Figure 2C and D, Euroimmun slides). Cerebrospinal fluid (CSF) analysis revealed a white blood cell count of14×10^6 cells/l with lymphocytic predominance, normal protein and glucose, negative cytology. Routine EEG showed intermittent bursts of mixed theta/delta slowing in the left centroparietal region. Brain biopsy showed gliotic brain tissue with marked mixed inflammatory infiltrate consisting of lymphocytes with scattered plasma cells. Radiographically, brain MRI in this disorder is usually unremarkable but focal enhancement or medial temporal lobe abnormalities have recently been reported [1, 2]. Both hypometabolism and hypermetabolism have been reported on FDG-PET [3, 4]. The imaging findings in our patient showed decreased metabolism and enhancement within the limbic system, as well as extension into the midline cortical structures. The anatomical abnormalities were consistent with the patient's motor and cognitive behavioral issues. The patient stabilized after treatment with high dose steroids followed by a five day course of intravenous immunoglobulin. He returned five weeks later for increased confusion and a seizure. Repeat testing for NMDA receptor antibodies was negative at that time by indirect immunofluorescence (titer <120), although positivity persisted on transfected cells (Euroimmun). A decision was made to treat with 5 weekly infusions of rituximab. Over the ensuing two months, the patient made a dramatic recovery and returned back to his baseline.

Affected individuals with NRA develop characteristic clinical features, including seizures and unresponsiveness, psychiatric symptoms with memory loss, dyskinesias, autonomic instability and hypoventilation. This autoimmune neurological disorder effects a disproportionate number of female children and adolescents and is most commonly associated with ovarian teratoma [5, 6]. In the current report, the effected individual had a similar clinical course but was male, an adult, and did not have an identified underlying malignancy by pan body CT imaging.

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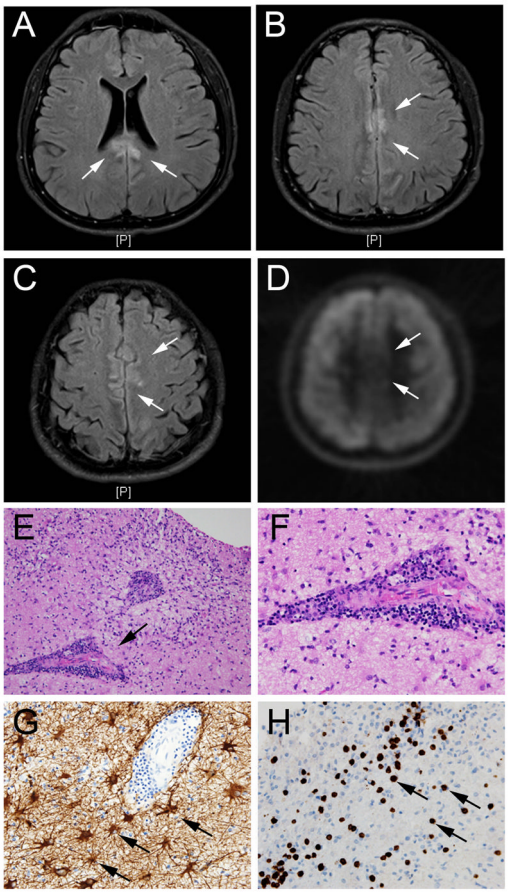

Figure 1.

Axial contrast enhanced FLAIR MRI of the brain (A–C) demonstrates involvement of the splenium of the corpus collosum and medial portion of the bilateral frontal and parietal lobes (white arrows). (D) FDG-PET demonstrates corresponding decreased metabolic activity (white arrows). E–F) Hematoxylin-eosin stained sections show markedly reactive brain tissue with prominent perivascular and intraparenchymal chronic inflammatory infiltrates (arrow) predominantly composed of mature lymphocytes and scattered plasma cells (100x, 400x). G) GFAP immunohistochemistry highlights reactive astrocytes (arrows, 400x). H) CD3 immunohistochemistry labels T cells (arrows, 400x).

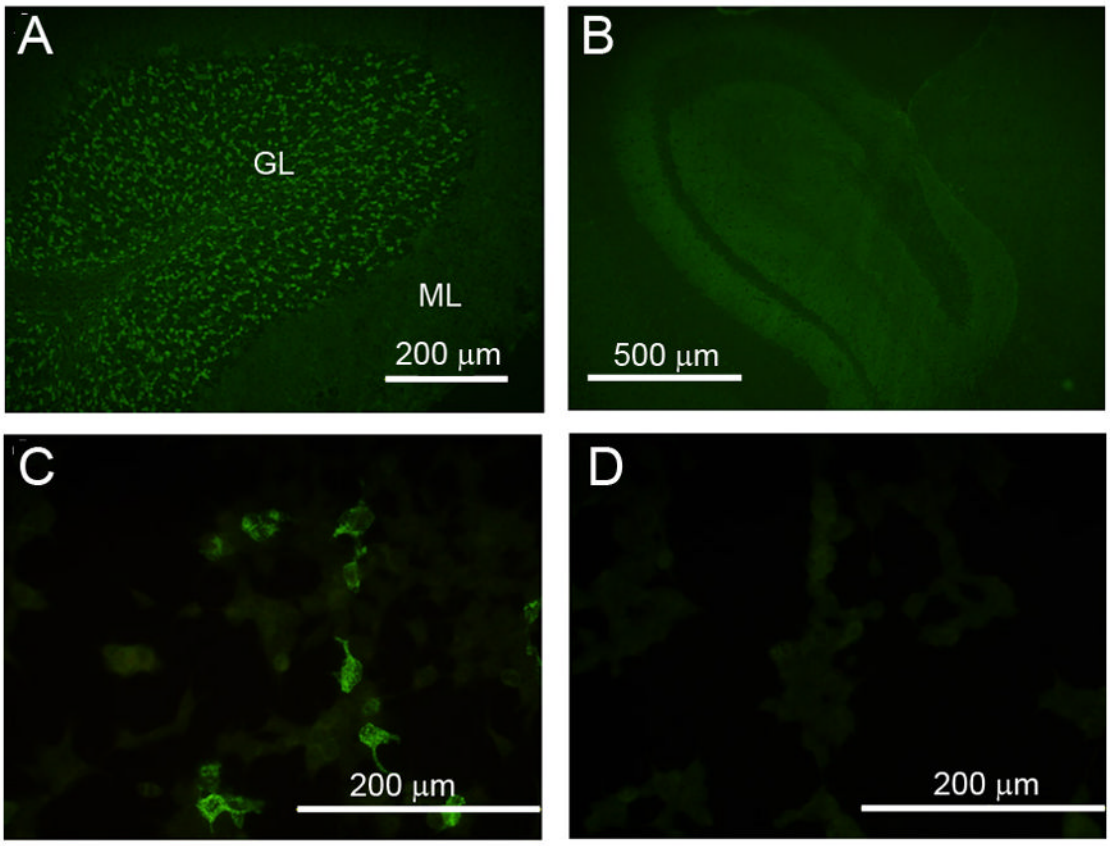

Figure 2.
Patient's serum (shown) and cerebrospinal fluid (not shown) contained IgG that bound synapse-rich regions of the molecular layer of the mouse hippocampus (A) and the granular layer of the mouse cerebellum (B) in a pattern consistent with NMDA receptor specific-IgG. Binding to NMDA receptor transfected HEK293 cells (C) but not untransfected cells (D) confirms specificity. (Provided by Vanda Lennon and Sean Pittock, Neuroimmunology Laboratory, Mayo Clinic, Rochester, MN)