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Clinical Observations

Limbic Encephalitis in a Child: An Atypical Presentation

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ABSTRACT

BACKGROUND: Limbic encephalitis is a rare disorder with a generally subacute onset evolving over days to weeks. Patients present with a variable combination of memory loss, seizures, and psychiatric disturbance, and it is not rare for patients to be initially misdiagnosed. **PATIENT:** We describe a previously healthy 12-year-old boy who developed his first seizures at 8 years of age. He had a total of eight prolonged focal seizures, each followed by a month of behavioral changes and short-term memory loss. There was no family history of seizures or other neurological disorders, and he had an otherwise unremarkable neonatal and medical history. **RESULTS:** Magnetic resonance imaging during each episode of seizures showed alternating unilateral brain hemispheric involvement consistent with limbic encephalitis that was followed by resolution for a total of six times. Despite a negative laboratory evaluation for a large panel of paraneoplastic antibodies, the clinical scenario and exclusion of other possible disorders made recurrent limbic encephalitis the most likely diagnosis. **CONCLUSION:** Limbic encephalitis is a rare disorder that is diagnosed primarily on the basis of clinical criteria and is often associated with the presence of a paraneoplastic antibody. However, lack of a positive paraneoplastic antibody in a patient with a triad of seizure, behavioral changes, and short-term memory loss does not exclude the diagnosis. The unique presentation in a seronegative patient may indicate an unrecognized antibody.

Keywords: limbic encephalitis, seizure, memory, antibodies, magnetic resonance imaging (MRI)

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Case Report

A 12-year-old boy was previously well with normal cognitive function until age 8, when he developed his first attack of seizure.

The patient's first seizure developed as sudden awakening from sleep with confusion. He vomited once and immediately developed right-sided clonic seizure with head and eye deviation to the right. This was followed by secondary generalization with loss of consciousness. It was aborted by anticonvulsant medication after 30 minutes. Magnetic resonance imaging (MRI) brain was normal (Fig 1A).

Within 4 years, the child had a total of eight status epilepticus episodes starting as focal seizures with secondary generalization. Each seizure was requiring an antiepileptic medication to be aborted and was followed by 3 weeks to a month of behavioral changes and short-term memory loss. His behavioral changes were in the form of apathy and unusual disrespect to his parents and people around him. He improved gradually after each attack, but never returned back to baseline.

His focal onset seizures were always accompanied by changes on brain imaging in the opposite hemisphere. Seizures one, two, three, five, and seven were right-sided with left temporal or temporoparietal lesions. His fourth, sixth, and eighth attacks were left-sided with right-sided temporoparietal lesions as per imaging (Figs 1 and 2).

After the first year of seizures, the patient started to have daily short seizures that were not associated with behavioral changes or short-term memory loss.

MRI of the brain one year after the sixth attack revealed bilateral temporal lobe abnormal signal intensity, loss of volume, and scattered cortical hyperintensities with evidence of meso-temporal sclerosis (Fig 2B). Positron emission tomography (PET) scan revealed mild diffuse bilateral cortical hypometabolism with small areas of relative hypermetabolism in the bitemporoparietal and mesial temporal cortices (Fig 3).

Neonatal and medical history was unremarkable. A maternal uncle had brief controllable seizures. Parents are not consanguineous, but they are from the same tribe. The child had normal development and good school performance until he developed his first seizure. Currently, he is

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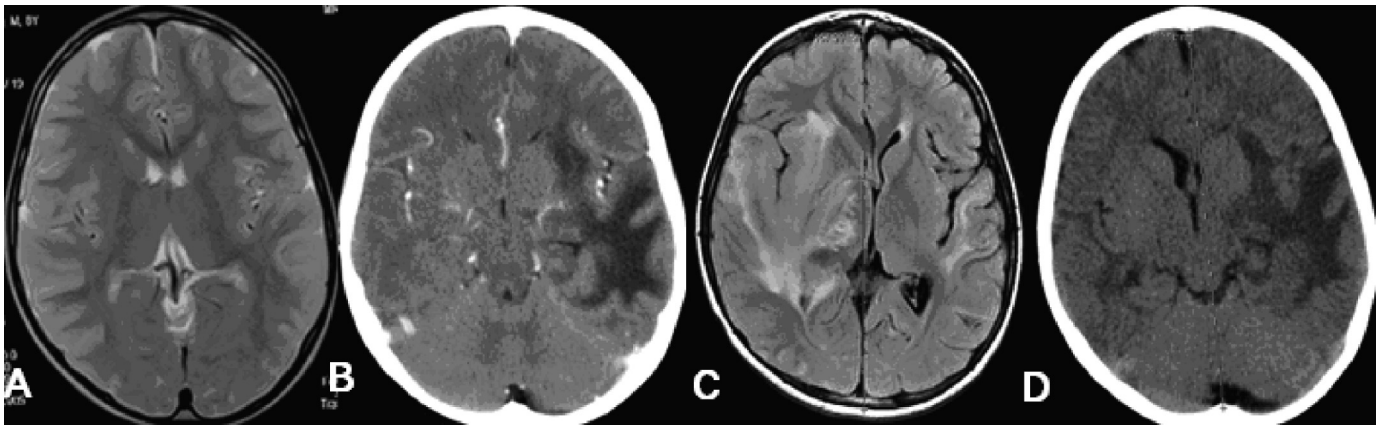

FIGURE 1.
(A) A normal magnetic resonance imaging (MRI) scan of the brain after the second attack. (B) Computed tomography (CT) scan brain after the third attack, revealed extensive white matter hypodensity in left temporal lobe. (C) An MRI scan of the brain after the fourth attack revealed new development of a large right temporal lobe lesion with of improvement of the previous left hemispheric lesion. (D) CT scan of the brain after the fifth attack revealed redevelopment of the left temporoparietal hypodense area with significant improvement of the previous right hemispheric lesion.

in 7th grade with poor performance and multiple school absences. He is fully vaccinated. He has unremarkable systemic examination apart from large 5- × 6-cm café au lait spot on the medial side of his right thigh.

Neurological evaluation after each attack revealed orientation impairment to time, place, and persons, with loss of spontaneous speech and inability to repeat phrases. Recent memory was impaired for about a month, which was confirmed by neuropsychiatric evaluation. Remote memory was intact. Examination of cranial nerves was normal, with temporarily, motor weakness, and exaggerated reflexes contralateral to the brain lesion. Sensory and cerebellar examination was difficult to perform during the illness because of a lack of cooperation, but it was normal between the attacks.

Hematological, biochemical, immunological, and infectious evaluations were unremarkable.

Serum paraneoplastic antibodies including ANNA-1 (anti-neuronal nuclear antibodies), ANNA-2, ANNA-3, AGNA (anti-glial nuclear antibodies), PCA (Purkinje cell cytoplasmic antibodies)-1, PCA-2, PCA-Tr, CRMP (collapsin response mediator protein)-5-immunoglobulin G, amphiphysin antibody (Ab), striated muscle Ab, P/Q-type calcium channel Ab, N-type calcium channel Ab, Ach receptor muscle-binding Ab, AchR ganglionic neuronal Ab, neuronal voltage-gated K+ channel Ab, anti-NMDA (N-Methyl-D-aspartate), and anti-AMPA (2-amino-3-[3-hydroxy-5-methyl-isoxazol-4-yl]propanoic acid) Ab were all negative.

Cerebrospinal fluid (CSF) oligoclonal bands and polymerase chain reaction herpes simples virus tests were negative, but CSF albumin and immunoglobulin G were high. Repeated electroencephalogram showed generalized slowing in some studies and focal slowing in others, with very rare epileptiform discharges. Computed tomography of the chest, abdomen, and pelvis were unremarkable apart from right undescended testis, which showed no malignancy in pathological examination. PET scan of the whole body revealed mildly hypermetabolic right paracolic and right groin lymph nodes. Visual- and auditory-evoked potentials during the attacks were normal. Brain biopsy from the right temporal lobe revealed significant profuse infiltration of the brain parenchyma with CD3- and CD8-positive T cells.

Based on the clinical scenario of memory loss, seizures, and psychiatric symptoms, the diagnosis of limbic encephalitis was considered and the child was treated accordingly by intravenous methylprednisolone for 5 days (30 mg/kg/day) and tapering doses of prednisolone. He showed good improvement.

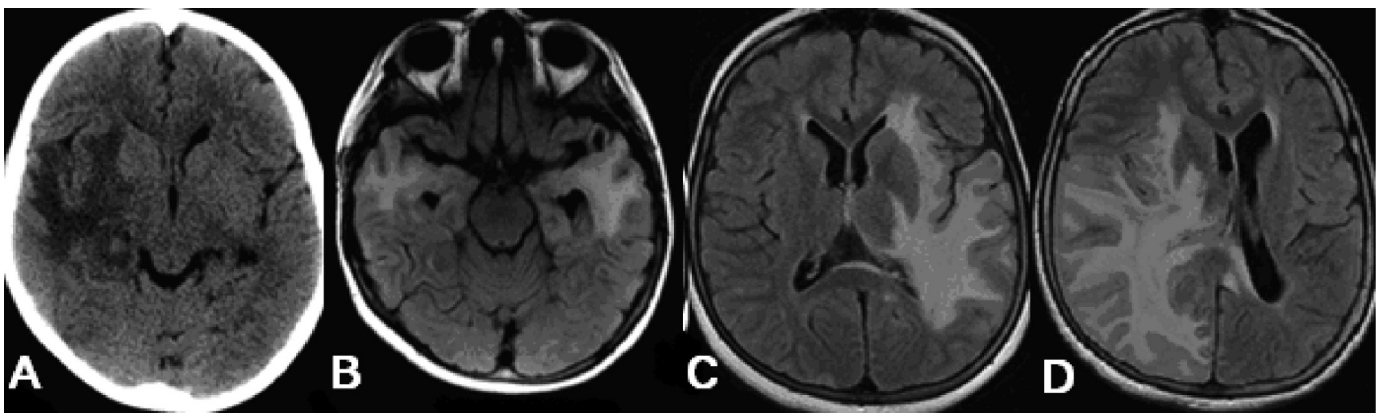

FIGURE 2.
(A) Computed tomography scan of the brain after the sixth attack revealed reappearance of right temporoparietal lesion and regression of the previous left hemispheric lesion. (B) A magnetic resonance imaging (MRI) of the brain a year after the sixth attack revealed bilateral temporal lobe abnormal signal intensity with evidence of mediotemporal sclerosis. (C) An MRI scan of the brain after the seventh attack showed reappearance of left temporoparietal lesion and regression of the previous right hemispheric lesion. (D) An MRI scan of the brain after the eighth attack revealed reappearance of right temporoparietal lesion and regression of the previous left hemispheric lesion.