MRI Is a Must in Children on Vigabatrin Therapy

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

PITTSBURGH — Children taking the anticonvulsant vigabatrin should have baseline and follow-up magnetic resonance imaging, because the drug has been associated with new-onset MRI hyperintensities in about 20% of those who take it, Dr. Phillip L. Pearl reported in a poster at the annual meeting of the Child Neurology Society.

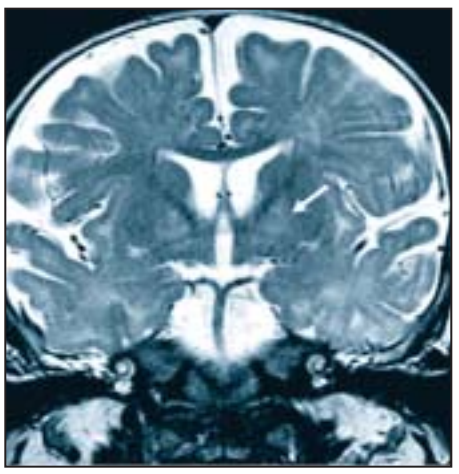
Although the drug has never received Food and Drug Administration approval—because it can cause retinotoxicity with visual field constriction in about 30% of patients—some patients do receive it for compassionate use or in Institutional Review Board–approved protocols, Dr. Pearl said in an interview. U.S. patients usually obtain it from Canada. Vigabatrin is widely available outside the United States.

"Our results seem to support the original preclinical concerns about this drug," said Dr. Pearl, a pediatric neurologist at the Children's National Medical Center, Washington.

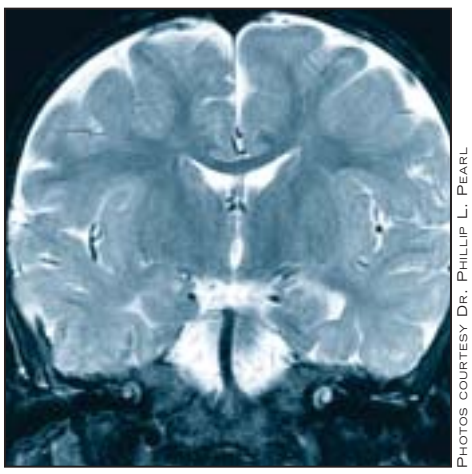
The drug irreversibly inhibits gamma-aminobutyric acid transaminase. He described vigabatrin's effects on imaging in 15 patients (aged 11 months to 11 years) who underwent MRIs while taking it. Diagnoses included tuberous sclerosis complex (five patients), cortical dysplasia (five), cryptogenic infantile spasms (two), Down syndrome (one), metabolic encephalopathy (one), and mesial temporal sclerosis (one).

All of the patients had abnormal MRI scans during the course of vigabatrin therapy. However, three infants with normal baseline scans (two with cryptogenic infantile spasms and one with Down syndrome, all aged 12-13 months) experienced new-onset, vigabatrin-related T2 hyperintensities, Dr. Pearl said.

In one patient with infantile spasms, the abnormal signal occurred in the basal ganglia, thalami, anterior commissure, and brainstem. The second patient, who had Down syndrome, experienced the increased signal in the thalami, tectum, and corpus callosum. The signal occurred in the brainstem, palladi, and dentate nuclei of the third patient, who had infantile spasms. Diffusion-weighted imaging indicated intracellular cytotoxic edema in all three.



A scan of basal ganglia of a child on VGB shows signal abnormality.



The signal abnormality resolved once the child discontinued VGB therapy.

PHOTOS COURTESY DR. PHILLIP L. PEARL

At the time of the abnormal scan, the mean dose of vigabatrin was 143 mg/kg per day, and the mean duration of therapy was just over 3 months. All of the abnormal signalling resolved when vigabatrin was discontinued. The abnormal scans in the other 12 patients were all related to their underlying diagnoses. The mean dose of vigabatrin at the time of their abnormal scan was 77 mg/kg per day, and the mean duration of therapy was 14 months.

Because the new-onset abnormalities appeared in very young patients, Dr. Pearl said, infants may represent a high-risk group and should be carefully followed by a neurologist. He said the abnormalities may be symptomatic, but he has not identified their clinical significance with certainty.

New-onset hyperintensities related to vigabatrin may be even more common, according to Dr. Pearl. ■

Deficits Linger in Pediatric Self-Limiting Leukodystrophies

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

PITTSBURGH — Two previously undescribed self-limiting leukodystrophies appear to affect infants and children, leaving them with residual neurologic deficits despite resolution of severe abnormalities of white matter with cavitations, Dr. SakkuBai Naidu, said at the annual meeting of the Child Neurology Society.

Dr. Naidu, director of the neurogenetics unit at the Kennedy Krieger Institute, Baltimore, described the disorders in eight children.

The first unnamed disorder she described occurred in six neonates, two of whom were monozygotic twins. All six infants developed neurologic symptoms within the first week of life. Apathy appeared initially, followed by lethargy and seizures requiring intubation. "The initial magnetic resonance imaging was not informative, except for abnormal diffusion-weighted imaging," she said in an interview. "However, 2 weeks later, the white matter developed large cystic cavitations throughout the corona radiata."

At that point, the infants had improved clinically, were weaned from ventilators, and placed on anticonvulsants. They later developed hypotonia progressing to mild spasticity, without recurrence of seizures.

Follow-up MRIs at 1 year showed complete resolution of the cavitations without significant brain atrophy. However, all the infants had cortical blindness and were developmentally delayed.

The second recently discovered leukodystrophy disorder was found in two older children who were healthy and developmentally normal until the second decade of life, Dr. Naidu reported. Initial symptoms were insidious, starting with progressive dementia, and then followed by dystonia, rigidity, and ataxia. Imaging showed a similar kind of bilateral cystic cavitation in the cerebellum with abnormal white matter.

By the end of the second decade of life, however, disease progression had stabilized. Imaging showed that the lesions had improved, although both children were left with residual rigidity, ataxia requiring aids for walking, and dementia.

"The most devastating MRI changes and clinical manifestations in the two conditions appear to have an age-associated onset, but self-limiting course, suggesting that timing identifies specific MRI changes, and time determines the clinical outcome in some disorders," Dr. Naidu said. ■

NIH Funds Web-Based Neuroimaging Tools Clearinghouse

The National Institutes of Health has awarded a 5-year, $3.8-million contract to establish the Web-based Neuroimaging Informatics Tools and Resources Clearinghouse. The clearinghouse, which will focus initially on functional magnetic resonance imaging, will hold neuroimaging tools, vocabularies, and databases, and will provide ongoing opportunities for public comment. For more information, visit www.neuroscienceblueprint.nih.gov. ■