Acquired Variant of Rett’s Disorder and Response to Lamotrigine

SIR: Although Rett’s Disorder (RD) is associated with a gene mutation, various phenotypes, including non-genetic variants, of this disorder have been described in literature.\(^1,2\) The diagnostic criteria for RD has evolved over time to include the variants of this condition.\(^2\) RD is traditionally considered a neuro-developmental disorder with acquired neurological conditions constituting an exclusion criterion.\(^3\) In contrast, other pervasive developmental disorders such as autistic disorder and childhood disintegrative disorder have been described with neurological conditions as per the DSM-IV TR. We report a case of a 5-year-old girl who developed a variant of RD as a sequel of encephalitis. In addition, the successful use of lamotrigine in treating some of the behavioral and autistic symptoms in patients with RD without any evidence of active seizures is underscored.

Case Report
A 5-year-old girl presented with a multitude of symptoms of a year’s duration characterized by autistic behavior, hyperactivity, stereotypic hand movements and developmental regression. The patient’s developmental history revealed a history of birth anoxia and delayed developmental milestones. By age four, her development was limited only to social smile, speaking 15–20 meaningful words, walking and running unaided, indicating for toilet needs, and some interactive play. At the age of 4 years, the patient was treated for an illness lasting 2 weeks characterized by high-grade fever, altered sensorium and two episodes of generalized tonic-clonic seizures. Although the parents were not sure of the diagnosis, the history was suggestive of encephalitis. Following recovery from the febrile illness, the mother noticed that the patient had lost most of her previous abilities. She started banging her head against the wall, became hyperactive, and had an unsteady gait. She lost all meaningful speech and made guttural sounds. Her reciprocal social interaction was severely inhibited and she would recognize only her mother. In addition, she developed bowel and bladder incontinence. Her mental state examination revealed inattentive, hyperactive and self-absorbed behavior. Notably, she held her hands in front of her chest in a dystonic posture and displayed stereotypic hand washing and hand-wringing movements. Neurological examination revealed a normal head circumference, hypotonia in limbs, loss of fine motor skills and a broad-based gait. Her EEG record was normal, but a CT head showed multiple hypodense areas in the brain indicative of brain insult from the febrile illness. Clonidine was started and titrated up to 0.3 mg/day with minimal improvement in hyperactivity and other behaviors. It was then tapered and discontinued and substituted by lamotrigine at 12.5 mg at night, which was increased to 37.5 mg/day over a period of 1 month. At this dose, the patient showed considerable improvement in the stereotypical hand movements, hyperactivity and self-injurious behavior. She started recognizing her other family members and would indicate with gestures when she was hungry and when she needed to go to the toilet. Her social behavior showed some improvement in terms of a better eye contact and greater awareness and interest in her surroundings. However, there was no improvement in her speech. She did not have any side effects with the medication.

Comment
This patient, though not meeting the DSM-IV TR criteria for classic RD in that her milestones were delayed to begin with and there was no deceleration in the head circumference, did show some other features suggestive of RD. The characteristic loss of purposeful hand movements, stereotypic hand washing movements with the arms flexed in front, and the ataxic gait, as in this patient, are more preva-
lent in RD than other autistic disorders. In addition, regression in speech, communication skills and social interaction is suggestive of a pervasive developmental disorder, which, taken together with the above observations and occurrence in a female are reminiscent of RD. It has already been argued that the prevailing diagnostic criteria for RD are too restrictive, which may exclude atypical or borderline variants of this condition. In addition, while autistic disorder and childhood disintegrative disorder are associated with acquired neurological disorders, the criteria and description of RD in DSM-IV TR are silent on this aspect. A recent update on diagnostic criteria for RD omitted the exclusion criterion of acquired neurological disorders in the revised criteria for variant phenotypes of this condition.

The other pertinent facet of discussion is the use of lamotrigine in RD. Kumandas et al. used lamotrigine in two girls with RD and found that apart from convulsions, lamotrigine also improved stereotypical hand movements and autistic behaviors as happened with our patient. Another study showed that lamotrigine enhanced social behavior, temper tantrums and emotional problems in some patients with RD. Besides RD, lamotrigine has been used, albeit with mixed results, in either autistic disorder or patients with intractable epilepsy showing autistic symptoms. One such open-label study showed a positive effect of lamotrigine on some autistic symptoms, while a placebo-controlled trial failed to show any such effect. Whether patients with RD present with motoric symptoms such as stereotypic hand movements, ataxic gait, and dystonic posturing which are differentially responsive to lamotrigine as compared to other autistic spectrum disorders, remains to be ascertained. Moreover, as lamotrigine is now known to be effective in certain affective disorders, whether RD patients with emotional dysregulation respond better to it, is worth exploring. This is suggested by decreased irritability and improved emotional stability in patients displaying autistic symptoms treated with this drug. More systematic studies are needed to address these issues. At a neurotransmitter level, there is some evidence to support the role of lamotrigine in RD. Glutamate is elevated in CSF of patients with RD and lamotrigine, by way of inhibiting release of glutamate, may be effective in ameliorating some of the symptoms of this rare condition.

DATTATREYA N. MENDHEKAR HARPREET S. DUGAL Tecumseh, Mich.

References

Neuroanatomical Changes After Eye Movement Desensitization and Reprocessing (EMDR) Treatment in Posttraumatic Stress Disorder

Several authors have found smaller hippocampal volumes in patients with PTSD and some have suggested that psychotropic drugs may promote hippocampus neurogenesis and reverse the decrease in hippocampus volume. However, the only study that has investigated the effects of psychotherapy on hippocampus volume failed to show a volumetric increase after effective psychotherapy.

EMDR is a standardized psychotherapy for amelioration of traumatic sequelae.

We evaluated the hippocampus volumetric changes after successful EMDR treatment of a 27-year-old man with a chronic PTSD related to the suicide of his mother. Written informed consent was obtained after the study procedures had been fully explained. The patient did not receive any medication during the 8 weeks of EMDR treatment. Current and lifetime PTSD diagnoses and severity were established by the Clinician Administered PTSD Scale (CAPS DX) and the severity by the Davidson Trauma Scale (DTS).

Morphovolumetric evaluation through high resolution MRI scanning (Philips 1.5T MRI) consisted of coronal T1 Fast Field Echo (matrix 512×512, 1 mm thick) images lying on the plane perpendicular to major hippocampal axis. Hippocampal volume was calculated using dedicated software (Analyze VW 1.16, BIR, Mayo Clinic, MN, U.S.) by manual delimitation of hippocampal shape according to Watson Laboratories, Inc. anatomical criteria on each slice where detected, by an operator.