

Original Letter

Familial Dysautonomia (Riley-Day Syndrome) May Be Associated With Epilepsy

To the Editor:

I am reporting a family of three children of Ashkenazi Jewish extraction, two of whom are monozygotic twins, with genetic confirmation of familial dysautonomia (FD) and atypical absence epilepsy.

A 9-year-old boy was born prematurely at 36 weeks; his neonatal period was complicated with respiratory distress and poor feeding. The twins were delivered by cesarean section at 37 weeks' gestation without complications. All three children had slow developmental milestones without regression. The oldest brother and twin B had febrile seizures; all of them had breath-holding spells; other events were described as momentary behavioral and speech arrest associated with eye fluttering. Video-EEG monitoring in all three captured absence-like events, associated with generalized 2.5-Hz spike and wave discharges. The absence-like seizures continue on a daily basis. Combination of topiramate (TPM) and ethosuximide (ESM) has been particularly effective. The older boy was seizure free on that regimen, and the twins improved but still persist with daily clusters of absence. There is no family history of FD.

The physical examination revealed low weight and height with mild dysmorphic features, elongated head, and high, arched, and narrow palate; the tip of tongue lacked fungiform papilla. Normal chest and spine but positive tibial torsion were seen. The tilt test is significant for erratic blood pressures with substantial postural changes and decreased heart rate variability during erect position. Cranial nerves are normal. The gross motor examination is normal, but they have a decrease of fine motor movements bilaterally. Coordination and gait are intact. The sensory examination in the older boy revealed abnormally decreased temperature perception (tested with ThermoTest by Nicolet), but the twins appeared to

have relatively good appreciation of temperature changes and other sensory modalities. Deep tendon reflexes are normal without Babinski.

The neurometabolic and genetic workup were essentially normal except for the presence of two copies of a DNA mutation at the IKAP (IkB kinase complex-associated protein) region, diagnostic of FD.

To my knowledge, this is the first time that FD has been associated with epilepsy. Although seizures have not been considered to be characteristic, ~40% of patients with FD will experience at least one seizure with extreme provocation such as hypotension, fever, hypoxia with infection or breath holding, or electrolyte imbalance (1). These children have a uniform age at onset, seizure type, EEG, seizure frequency, and their seizures were not triggered by provocation, which suggests an epileptic syndrome. The seizures were brief and sometimes confused with dysautonomic crisis. One of the twins has cortical dysplasia, but the other two children do not have a clear predisposition for seizures. In addition, two of them had febrile convulsions. Multiple genes have been associated with epilepsy; therefore it is feasible that genetic abnormalities in FD also may predispose the susceptibility for epilepsy. Autonomic crisis may mask the presence of absence seizures; therefore I suggest screening those patients with EEG, neurologic consultation, and video-EEG monitoring if available.

I hope this report increases awareness of care providers of people with FD and this possible association, and that they screen those patients accordingly.

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REFERENCE

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