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Opsoclonus-Myoclonus Presenting With Features of Spasmus Nutans

Spasmus nutans designates an early childhood clinical triad of nystagmus, head nodding, and torticollis.[1–11] The head nodding and tilt are variably present; the nystagmus consists of fine, usually continuous, pendular oscillations, the amplitude of which changes from moment to moment and usually differs in the two eyes. One eye may show no oscillations at all.[1,3,5,8–10] Initially believed to represent an idiopathic, self-limited illness lacking other neurologic or constitutional manifestations, spasmus nutans has recently been linked to gliomas of the optic nerve and chiasm[2,4,5] and hypothalamus,[10,12,13] ependymoma of the fourth ventricle,[2,11] obstructive hydrocephalus,[2] and Leigh disease.[14] In order to point out how misleading the diagnosis of spasmus nutans may be, we present a patient who initially manifested a low-amplitude, high-frequency nystagmus, head nodding, and torticollis and weeks later progressed to an unmistakable opsoclonus-myoclonus syndrome.

Case Report

An 11-month-old girl developed bilateral otitis media and fever followed 1 week later by head tilt and tremor, irritability, and unsteadiness when sitting up. The side-to-side head tremor disappeared when she slept. She was the product of a full-term, normal gestation and normal delivery, and had no family history of neurologic disease.

Physical examination revealed an irritable but consolable child with normal vital signs, weighing 8.2 kg (20th percentile) and having a head circumference of 44.2 cm (20th percentile). Her head, tilted to the left, shook from side to side intermittently. Both eyes showed small-amplitude, high-frequency intermittent horizontal, vertical, and oblique eye movements in all positions of gaze, including straight ahead (primary) position. Cranial nerve examination was otherwise normal. She had increased axial and appendicular tone, mild truncal titubation when she tried to sit, and dysmetria when reaching out for a toy. Deep tendon reflexes were hyperactive, and plantar reflexes were extensor.

Although the eye movements and torticollis suggested a diagnosis of spasmus nutans, the presence of other neurologic features impelled a full evaluation. Computed tomographic and magnetic resonance imaging scans of the brain were normal, and cerebrospinal fluid was acellular, with normal chemistries. A 24-hour urine collection revealed vanilmandelic acid, 1.9 mg/total volume (normal, 1 to 1.5 mg); homovanillic acid, 1.4 mg/total volume (normal, 0 to 4 mg); homovanillic acid/creatinine ratio, 17 mg/g of creatinine (normal, < 35 mg/g); epinephrine, 7.0 μg/total volume (normal, 0 to 5.0 μg); and norepinephrine, 8.0 μg/total volume (normal, 0 to 20 μg). Chest and abdominal computed tomographic and radiolabeled metaiodobenzylguanidine scan did not show neuroblastoma.

The child's head tremor worsened over the ensuing 2 weeks to the point of interfering with her sleep. Her parents now noted large involuntary eye movements, increasing unsteadiness, and rapid jerking of the extremities that interrupted her attempts at feeding. Examination showed rapid, continuous horizontal, vertical, and oblique conjugate eye movements of much higher amplitude than weeks earlier—features typical of opsoclonus. She manifested appendicular and truncal ataxia and frequent myoclonic jerks involving all extremities.

After a 7-day course of 40 units/day of intramuscular adrenocorticotrophic hormone, the amplitude of the eye movements, head tremor, myoclonus, and ataxia markedly decreased. By 6 weeks after treatment, she had fully recovered.

Discussion

In our patient, the combination of low-amplitude, high-frequency nystagmus, head nodding, and torticollis was compatible with spasmus nutans, but within weeks, the eye movements had evolved into opsoclonus, a saccadic eye movement disorder characterized by conjugate excursions of the eyes in any direction.[15] The excursions are arrhythmic, of large amplitude, and similar in the two eyes. In children, opsoclonus is often associated with head and trunk oscillation, extremity ataxia, and myoclonic jerks as a manifestation of an occult neuroblastoma or a previous viral illness (opsoclonus-myoclonus syndrome, or dancing eyes–dancing feet).[16] A low-amplitude eye movement disorder such as our patient initially displayed has not been described in opsoclonus, but one patient did show a diminution in amplitude after resection of a retroperitoneal neuroblastoma.[17] Normal individuals may manifest low-amplitude ocular flutter, a disturbance akin to opsoclonus.[18]

Our patient's eye movements did have two features that are considered uncharacteristic of spasmus nutans: movements of equal amplitude in the two eyes and movements in more than one plane. The nystagmus of spasmus nutans is usually horizontal, less commonly vertical, and much less commonly both. However, these features are difficult to discern in an irritable infant whose head is shaking. Considering the prominent torticollis, a characteristic of spasmus nutans but not opsoclonus-myoclonus, it is no wonder that examiners strongly considered the diagnosis of spasmus nutans.

Our case is, as far as we know, the first to link features of spasmus nutans and opsoclonus-myoclonus. It points out the difficulty in distinguishing between a fine pendular rhythmic ocular oscillation and a nonrhythmic saccadic intrusion and suggests the possibility that they have a common generator. It also serves as a reminder that the proper classification of spasmus nutans remains in doubt. The typical pattern of uniplanar sinusoidal (pendular) oscillations with varying rhythms and dissociated amplitudes and frequencies in the two eyes has been described both as an apparently isolated phenomenon and as a manifestation of tumors, infections, and developmental abnormalities of the central nervous system. Neither the clinical nor the electronystagmographic examination can distinguish between the benign, isolated condition ("pure" spasmus nutans) and that associated with other neurologic manifestations.[2] Curiously, this eye movement abnormality is quite different from that found in most acquired disorders affecting the brain stem in childhood, which typically cause either (1) a jerk nystagmus in side and upgaze and no nystagmus in the straight ahead (primary)

position or (2) circular or oval pendular oscillations (as in Pelizaeus-Merzbacher disease[19] and multiple sclerosis[20,21]).

We suggest that spasmus nutans be considered not a diagnostic entity, but a manifestation of a brainstem disturbance with manifestations sometimes not readily appreciated because of the difficulty of examining a small child or until the disease evolves. Thorough, repeated clinical examination and brain imaging are appropriate.

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Baclofen in the Treatment of Polymyoclonus in a Patient With Unverricht-Lundborg Disease

Unverricht-Lundborg disease is characterized by progressive ataxia, polymyoclonus, seizures, and intellectual deterioration.[1] It was first described by Unverricht in 1891. Lundborg, Unverricht's student, reported 50 similar cases in 30 families in 1903.[2] Valproic acid and/or clonazepam have been reported to be effective in ameliorating the polymyoclonus and seizures seen in Unverricht-Lundborg disease.[3–6] In our patient, however, these drugs were ineffective in modifying the polymyoclonus and ataxia.

Case Report

A.B. is a 15-year-old right-handed girl who was born in Poland after a full-term gestation followed by a normal spontaneous vaginal delivery. She walked at 14 months and spoke in phrases by 25 months. At 3 years of age, she had a generalized seizure with fever. She recovered spontaneously, and no treatment was prescribed. At 4 years of age, she developed an ataxic gait, which became progressively worse. By age 5 years, her parents had noted mental deterioration and slurred speech. Intention polymyoclonus was first noted at age 6 years. All of her symptoms deteriorated, so that by age 11 years she was wheelchair bound and was unable to feed herself. Her father had to pick her up to move her from place to place. She was withdrawn and depressed, and her speech had become totally unintelligible.

The family emigrated to the United States in November 1992, when the patient was 15 years old. Two weeks later, on November 24th, she was admitted to Bellevue Hospital. On admission, she was taking ethosuximide 250 mg qid, vitamin B_{12}, valproic acid 250 mg tid, and clonazepam 2 mg tid. She was having four or five generalized and myoclonic seizures per day. General physical examination was normal. There was no hepatomegaly. Neurologic examination revealed a depressed child strapped into a wheelchair. Although she made sounds, her speech was unintelligible, and she did not follow commands even when given by her parents. At rest, there was titubation and constant diffuse polymyoclonus made worse by intention. She was able to hold a pencil with a palmar grasp, and her drawing and handwriting were unintelligible (Figure 1A). Hypertonia was present in all four extremities. Deep tendon reflexes were increased throughout. However, toes were bilaterally down-going. She had severe truncal and appendicular ataxia made worse with intention.

Work-up including complete blood count, sequential multiple analysis–7, Mg^{++}, PO_4, liver function tests, lactic acid, analysis of cerebrospinal fluid (white blood cells, protein, glucose, lactate, and pyruvate), carnitine (total and free), vitamin E, serum α-tocopherol, rubeola immunoglobulin G, and blood and urine organic amino acids produced normal results. Skin biopsy for Lafora bodies and neuronal ceroid lipofuscinosis was normal. Electron microscopy showed normal mitochondria architecture. Studies for G_{M1}, G_{M2}, and α-(*N*)-neuraminidase were normal. Head computed tomographic scan with contrast, electromyogram, and brainstem auditory evoked responses were normal. Electroencephalogram showed diffuse slowing with occasional parasagittal spikes. Visual evoked response showed abnormal P100 waves bilaterally. Ethosuximide and vitamin B_{12} were discontinued, with no change in her clinical status. Her valproic acid level was 85 μg/mL on 250 mg tid. The valproic acid dosage was raised to 500 mg tid, with a blood level of 120 μg/mL and no change in her clinical status. In order to attempt to decrease hypertonia and spasticity, baclofen 40 mg/day was added and gradually increased to 150 mg/day. Polymyoclonus and ataxia were significantly decreased, as was the spasticity and hypertonia. This resulted in a remarkable improvement in her clinical condition, so that she is now able to stand alone, walk holding on with one hand, climb steps, and turn while walking. She can throw and catch a ball and go on a swing and move it without assistance. She can draw pictures (Figure 1B), write legibly (Figure 2), use scissors, and feed herself. Speech is now intelligible, with a higher than expected cognitive level. She is outgoing and happy. Seizure frequency has decreased from four or five per day to one per week. This improvement has been sustained for 16 months to date.