

# Clinical Reasoning: A case of abnormal eye movements in an infant

## More than meets the eye



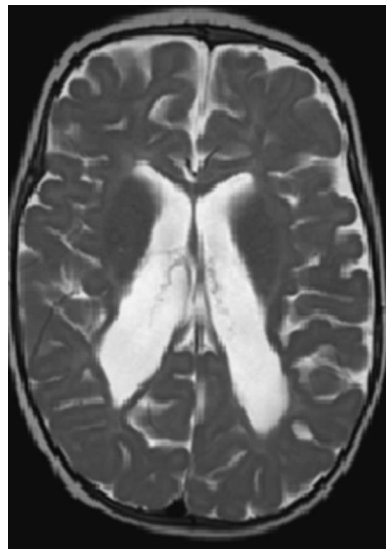
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### SECTION 1

The patient is a 9-month-old preterm boy (31 weeks gestational age) with infantile spasms for whom consultation was requested to assess new-onset abnormal eye movements.

**Figure** MRI brain



Axial T2 MRI brain demonstrates severe periventricular white matter volume loss bilaterally, particularly in the peritrigonal regions. There is associated increased periventricular T2 signal.

The pregnancy was complicated by antenatal hemorrhage at 29 weeks from placenta previa. The patient developed late fetal decelerations necessitating emergency caesarean section at 31 weeks. He was depressed at birth, requiring intubation. He spent approximately 8 weeks in the neonatal intensive care unit, primarily for feeding. Since birth, the child had been globally developmentally delayed and had gradually developed a spastic diplegic cerebral palsy. At age 8 months, the child developed paroxysmal flexor spasms occurring in clusters consistent with infantile spasms. EEG confirmed hypsarrhythmia. The patient was diagnosed with symptomatic West syndrome. MRI brain performed at that time demonstrated periventricular leukomalacia consistent with a perinatal hypoxic ischemic injury (figure). The patient was started on vigabatrin with subsequent resolution of clinical spasms and normalization of his EEG.

At approximately 9 months of age, while still treated with vigabatrin, the patient developed new paroxysmal, stereotypical abnormal eye movements lasting seconds to minutes, often occurring when first awakening (see the video on the *Neurology*<sup>®</sup> Web site at [www.neurology.org](http://www.neurology.org)).

### Question for consideration:

1. What is your differential diagnosis?

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## SECTION 2

There is tonic downward deviation of the eyes, with the eyes held in a slightly exotropic position. There are intermittent, nonrhythmic upward saccades, either purely vertical or oblique to either side.

Paroxysmal abnormal eye movements could be seizure-related, although typically vertical eye deviation in seizures is upwards due to activation of bilateral frontal eye fields. While a dorsal midbrain Parinaud syndrome is also associated with downward gaze deviation, there is often an associated lid retraction, light-near dissociation of the pupillary reaction, and a more persistent upward gaze palsy in severe cases. There is also a phenomenon in infancy termed the “eye popping” reflex that consists of a downward deviation of the eyes associated with lid retraction lasting seconds that is triggered by dimming the ambient lighting.<sup>1</sup> This reflex

may be present in the neonatal period and peaks at 14–18 weeks of age. Forced downward eye deviation with convergence has also been described in association with thalamic hemorrhage in adults and acute intraventricular hemorrhage in neonates.<sup>2</sup> Ocular dipping (inverse bobbing) and upbeat nystagmus can also cause a slow downward phase with a fast upward jerk, but these tend to be more rhythmic and the slow phase is not held in a tonic down-position. Finally, a transient phenomenon of paroxysmal isolated tonic downgaze in infants has been previously described by various authors.<sup>1,3–6</sup>

### Questions for consideration:

1. What other features would you look for on examination?
2. What investigations would you order?

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### SECTION 3

On ophthalmologic examination of our patient between episodes, the patient showed decreased visual interest and would not fix and track. Visual fields could not be assessed. Pupils were normally reactive. Slit-lamp examination of the anterior segments was normal. Dilated funduscopy showed only mild attenuation of the retinal nerve fiber layer bilaterally. The eye movements were conjugate in all cardinal positions of gaze. Vestibulo-ocular movements were full by doll's head maneuver. There was no associated lid retraction.

In patients with intermittent tonic downgaze, EEG should be considered to assess for seizures. If the events are happening on a daily basis, prolonged video-EEG can be arranged to capture the clinical events and more definitively exclude the possibility of seizures. Imaging of the brain, ideally with MRI, is also important to rule out a structural lesion. An electroretinogram (ERG) could be considered to evaluate for retinal disease.

In our patient, events were captured on video EEG and were not associated with electrographic seizure activity. EEG background was slow for age, but there were no interictal epileptiform discharges. Repeat MRI demonstrated no interval changes. Ganzfeld ERG was normal.

**DISCUSSION** Over the first year of life, the visual and oculomotor systems undergo great changes in the process of maturation. The fovea matures over the first few months of postnatal life. Cerebral myelination takes place primarily over the first 2 years of postnatal life; in the first 2 months, the optic nerves, tracts, and radiations are myelinated and by 4 months, the pericalcarine white matter in the occipital lobe is myelinated.<sup>5</sup> In addition to the primary geniculocalcarine visual pathway, there exists a parallel, subcortical visual pathway (the extrageniculocalcarine pathway) that functions transiently in the neonate as the geniculocalcarine cortex is developing. This pathway projects from the optic tracts to the pulvinar and superior colliculus, and ultimately to the visual cortex. This pathway may persist if there is significant injury to the geniculocalcarine pathway.<sup>5</sup> Cranial nerves III, IV, and VI are myelinated starting in the fifth postnatal month.<sup>7</sup> The precise timing for myelination of the supranuclear oculomotor pathways for smooth pursuit and saccadic eye movements is less certain, but maturation of smooth pursuit eye movements usually peaks over the first 6 months of life.<sup>8</sup>

The phenomenon of paroxysmal tonic downgaze is a poorly understood supranuclear disorder of gaze that has been reported in the literature in several forms. An idiopathic form has been described as a

benign, transient phenomenon in term infants resolving by 6 months of age with no ophthalmologic or neurologic sequelae and normal neuroimaging.<sup>3</sup> Typically there is no trigger for events, although there is a reported case in a 2-month-old child that began in the context of an intercurrent upper respiratory infection.<sup>4</sup>

A form of paroxysmal tonic downgaze has similarly been described in a series of extreme preterm infants (born between 22 and 28 weeks gestational age), developing between 36 and 38 weeks gestational age. In the latter series, episodes were often provoked by stimuli or feeding. The authors theorized that this transient phenomenon could result from delayed myelination of cortico-mesencephalic vertical eye movement pathways or immaturity or dysfunction of the extra-geniculocalcarine visual pathways.<sup>5</sup>

Symptomatic paroxysmal tonic downgaze has been described in association with CNS injury. One group reviewed a series of 10 preterm babies and 3 term babies between 2 and 8 months corrected age with a history of hypoxic-ischemic injury who demonstrated the phenomenon. All the preterm babies had spastic diplegia/quadruplegia and developmental delay, and most had visual impairment. In all the preterm babies, imaging demonstrated periventricular white matter volume loss with a predisposition for the peritrigonal/occipital horn regions containing the optic radiations. They documented in their population that the abnormal eye movements decreased with age, although some patients continued to have episodes at last follow-up (up to 5 years of age).<sup>6</sup> Another group has examined oculomotor abnormalities in term and preterm babies with cortical and subcortical (optic radiations and thalamus) visual loss. They found that tonic downgaze, esotropia, and optic nerve hypoplasia/pallor were more common with subcortical visual loss, whereas horizontal gaze deviation, exotropia, and normal optic disc appearance were more common with cortical visual loss.<sup>2</sup> Subcortical visual loss is more common in preterm babies due to a selective metabolic vulnerability of the periventricular preoligodendrocytes to hypoxic injury, with resultant periventricular leukomalacia.<sup>2</sup> Preterm babies with periventricular leukomalacia are also predisposed to a number of additional ophthalmologic abnormalities, including higher order visual processing deficiencies, visuospatial abnormalities, visual field loss (often inferior quadrants), esotropic strabismus, and abnormal extraocular movements.<sup>2</sup>

Recommended follow-up for patients with paroxysmal tonic downgaze depends on clinical context. Patients whose visual abnormalities are symptomatic of an underlying injury warrant close neurodevelopmental and ophthalmologic surveillance.

Paroxysmal tonic downgaze of infancy may represent an underrecognized syndrome that may ultimately

offer insights into the normal development of the geniculocalcarine and extra-geniculocalcarine (subcortical) visual pathways.

### AUTHOR CONTRIBUTIONS

Dr. Lance H. Rodan: preparation of manuscript, discussion. Dr. Ingrid Tein: revision of manuscript, discussion. Dr. Ray Buncic: revision of manuscript, discussion.

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### DISCLOSURE

The authors report no disclosures relevant to the manuscript. Go to [Neurology.org](http://Neurology.org) for full disclosures.

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