Paroxysmal Tonic Upgaze in Pediatric Patients with Down Syndrome: A Case Series

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Abstract

Paroxysmal Tonic Upgaze (PTU) is a paroxysmal movement disorder characterized by episodes of sustained upward deviation of the eyes, which can be misidentified as a seizure. There has been no definite association made between PTU and Down syndrome, although Down syndrome has been associated with various other ocular and neurologic conditions. This case report describes three patients with Down syndrome who presented with seizure-like activity and were ultimately diagnosed with PTU. Consideration of PTU in a differential diagnosis, especially in patients with a history of Down syndrome, is essential for accurately distinguishing potentially benign conditions from epilepsy and can help clinicians avoid misdiagnosis and unnecessary treatments.

Introduction

- **Paroxysmal Tonic Upgaze (PTU)** is a rare pediatric movement disorder characterized by **episodes of sustained upward deviation of the eyes with compensatory neck flexion, downbeating saccades with attempted downgaze, and normal horizontal eye movements**[1, 2].
- Onset typically occurring in those under one year of age, and may be triggered by febrile illness, fatigue or anxiety, and can be relieved by sleep[1,2].
- Diagnosis is supported by normal neurological examination, EEG and neuroimaging, making PTU easily mistaken for seizure activity[1,2].
- Down syndrome has been associated with a variety of other ocular findings including infantile nystagmus, strabismus, amblyopia, cataracts, refractive and accommodation errors, and glaucoma[3,4].
- PTU has not previously been reported in association with Down syndrome.
- ***We present three cases of PTU in patients with Down syndrome at a single center over last four years.***

References

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Patient 1

- 2-year-old African American female with Down syndrome, prematurity (35wk), and left SVC.
- At 2 months: episodes of staring, pallor, and spitting up with back-arching lasting 3-4 minutes.
- At 13 months of age: Recurrent episodes of whole-body stiffening with upward eye deviation lasting 1-2 seconds.
- No loss of consciousness or postictal state, approximately 3 episodes per week.
- Episodes triggered by excitement or emotional upset.
- Two video EEGs were normal for age; episodes were not documented as captured during monitoring.
- No neuroimaging obtained.
- Treated with famotidine for presumed GERD due to associated spit-ups and back-arching.

Patient 2

- 2-year-old Caucasian male with Down syndrome, di-di twin, GERD, laryngomalacia, RAD, and bilateral hypermetropia .
- At 15 months: seizure-like activity during an outpatient speech therapy session characterized by unresponsiveness, upward eye gaze, facial grimacing, and stiffening of extremities
- Episodes continued intermittently for approximately 5 minutes, after which the patient returned to baseline.
- Shortly thereafter: Clusters of rapid, forced eye closure, forward head jerking, and eyes rolling backwards, lasting 1-3 seconds per episode.
- Labs including CBC, CMP, and urine toxicology were unremarkable.
- CT head without contrast was normal.
- Video EEG monitoring showed epileptiform abnormalities correlated to stereotyped behavior and mild generalized background slowing, consistent with diffuse cerebral dysfunction.
- Episodes continued to be associated with feeds. He continued to work with speech therapy as episodes were associated with feeds and remained on anti-reflux medication.
- Episodes have since self-resolved.

Patient 3

- 4-year-old Caucasian female with Down syndrome, OSA, constipation, congenital heart defects.
- Family history of epilepsy in the patient's mother.
- At 3 years of age: episodes of unresponsiveness, stiffening of both arms and legs, eyes rolling back, and falling forward resulting in chin laceration.
- The episode reportedly lasted 15-20 seconds, with a subsequent 5–10-minute period of confusion.
- Video EEG showed left central vertex epileptiform discharges during sleep, although no corresponding events were noted, and changes were not present in the awake state.
- No neuroimaging obtained.
- Neurology recommended monitoring without anti-seizure medications, with repeat vEEG if events reoccur.
- Episodes self-resolved, and no further vEEG studies were performed. The reported confusion following the patient's episode was attributed to fatigue rather than a postictal state.

	Patient 1	Patient 2	Patient 3
Sociodemographic	2 years old African American Female	2 years old Caucasian Male	4 years old Caucasian Female
History	Down syndrome Preterm (35wk) Left SVC	Down syndrome Di-di twin GERD Laryngomalacia RAD Bilateral hypermetropia	Down syndrome OSA Constipation Congenital cardiac defects
Presentation	Body stiffening Staring episodes with pallor Eyes rolled backwards	Stiffening of extremities Eyes rolled backwards Facial grimacing Association with feeds	Stiffening of extremities Eyes rolled backwards Unresponsive episode Laceration secondary to above activity
Evaluation	vEEG (x2)	CT head w/o contrast vEEG	vEEG
Follow up	Self-resolution of symptoms		

Scan here for a video example of PTU.

Discussion

- Three pediatric patients with Down syndrome presented with stereotyped episodes of extremity stiffening, upward gaze deviation, and preserved consciousness.
- Neurologic evaluations, including video EEGs, were unrevealing and favored PTU over epilepsy.
- PTU is a rare disorder of unknown etiology; proposed mechanisms include upper dorsal brainstem dysfunction[2], immaturity or depletion of a neurotransmitter, an unrecognized channelopathy[2], or a cerebellar disorder[3].
- Neurodevelopmental differences in Down syndrome, including altered synaptic transmission, decreased neurogenesis, reduced plasticity, and other aberrant processes[5] may contribute to PTU susceptibility.
- Epilepsy remains an important differential diagnosis, given its increased prevalence in Down syndrome[5].
- PTU is different from epilepsy in that it is limited to eye symptoms, has no postictal period, and has a lack of spike activity on EEG during the upgaze episodes[2].
- PTU is a diagnosis of exclusion, requiring both the characteristic symptoms and lack of evidence for epilepsy.

Management & Prognosis

- PTU is generally benign and usually resolves spontaneously within 1-4 years[1].
- Anticonvulsants, acetazolamide, and ACTH have been shown to have no benefit and are not recommended[2].
- Individual patients have been noted to improve on levodopa, but routine treatment with levodopa is not recommended[1].
- Recognition of PTU may prevent unnecessary antiepileptic therapy and associated adverse effects.

Conclusions

- This case series describes three patients with Down syndrome whose clinical presentations were consistent with PTU.
- PTU should be considered in patients with Down syndrome presenting with seizure-like episodes and normal neurologic evaluations.
- Further studies are needed to determine whether an association exists between PTU and Down syndrome and to better define its prevalence.

Limitations

- Variability between the evaluations.
- Differences in duration and number of video EEG studies.
- Uncertainty regarding event capture during EEG monitoring.
- Incomplete availability of neuroimaging.
- Ongoing clinical follow-up may reveal alternative diagnoses or contributing factors.

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