Paroxysmal Tonic Upgaze: Physiopathological Considerations in Three Additional Cases

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Original Article

Paroxysmal Tonic Upgaze: Physiopathological Considerations in Three Additional Cases

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ABSTRACT

Paroxysmal tonic upgaze of childhood has been described as a benign distinctive syndrome of abnormal ocular movement, with or without concomitant ataxia. After the first observation of four children, a further 29 patients have been reported with a wide spectrum of neurologic abnormalities such as ataxia, unsteady of gait, learning disabilities and mental retardation at follow-up. Electroencephalograms were normal in all the subjects and magnetic resonance imaging showed deficient myelination in only one patient. Recently it has been suggested that paroxysmal tonic upgaze could be a heterogeneous syndrome, ranging from a simply age-dependent manifestation to a clinical appearance of a variety of disorders affecting the corticomesencephalic loop of vertical eye movement. Moreover, it also could be an early sign of more widespread neurologic dysfunction. We describe three patients who presented paroxysmal tonic upgaze; in one, ataxia was present; in the second child, ataxia and language disorder also were observed; and in the third patient paroxysmal tonic upgaze was associated with loss of muscle tone (drop-attack-like events). On magnetic resonance imaging, a pinealoma compressing the dorsal mesencephalic region was detected. On the basis of our observations, we suggest that any insult with periaqueductal mesencephalic gray-matter involvement could be considered the basic condition for this peculiar clinical manifestation. (*J Child Neurol* 2000;15:15–18).

Paroxysmal tonic upgaze of childhood has been described as a benign, distinctive syndrome of abnormal ocular movement, with or without concomitant ataxia. In all the first reported children, neuroimaging and electroencephalograms (EEGs) were normal, and at follow-up no mental retardation was observed.[1] After that first observation of four children, a further 29 patients have been reported. Among these 33 patients, 17 infants had a wide spectrum of neurologic abnormalities such as ataxia, unsteady gait, learning disabilities and mental retardation at follow-up. EEGs were normal in all subjects and magnetic resonance imaging (MRI) showed deficient myelination in only one patient.[2] Severity of the disorder was variable and in only a minority of cases was treatment used (corticosteroids, levodopa, benzodiazepines, drugs for intracranial hypertension), and not always successfully. The method of inheritance could be familial (dominant or recessive) or sporadic.[1–11] Recently, on the basis of the description of a group of 16 children,[10] it has been suggested that paroxysmal tonic upgaze could be a heterogeneous syndrome with respect to associations and outcome. Furthermore, it could be considered simply an age-dependent manifestation of a variety of disorders affecting the corticomesencephalic control of vertical eye movement. Nevertheless, it also could be an early sign of more widespread neurologic dysfunction.[10]

We observed three patients who presented paroxysmal tonic upgaze; in one, ataxia was present; in the second child, ataxia and language disorder were observed; and in the third patient loss of muscle tone (drop-attack-like events) was present. On MRI a pinealoma compressing the dorsal mesencephalic region was detected.

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CASE REPORTS

Case 1

A boy aged 4 5/12 years was the only child of nonconsanguineous healthy parents. Pregnancy and delivery were uneventful. The boy came to our attention at the age of 14 months because of unsteady gait, bouts of sudden upward deviation of the eyes, and sporadic

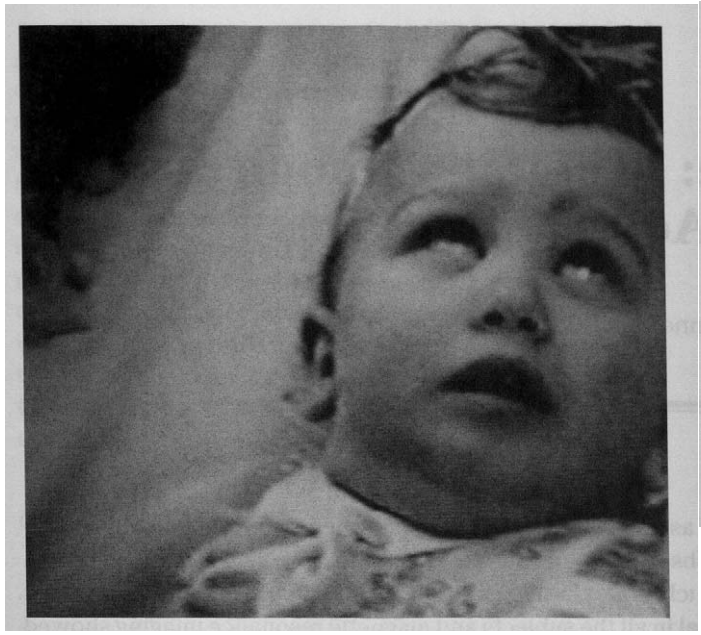

Figure 1. Episode of sudden upward deviation of the eyes.

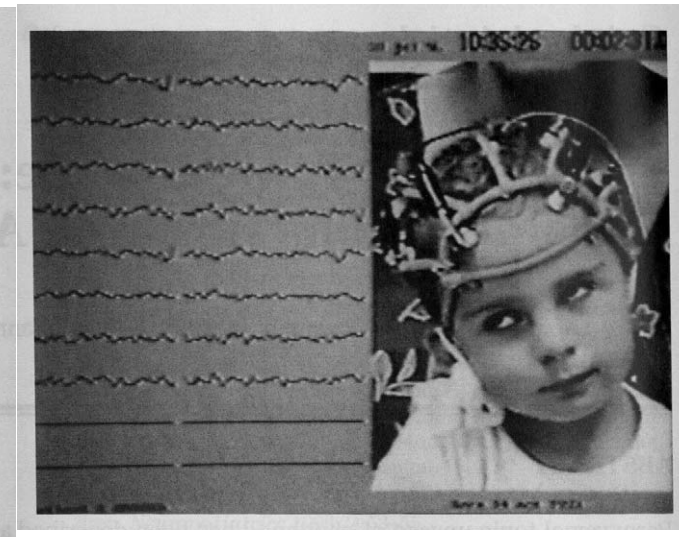

Figure 2. Sudden episode of paroxysmal tonic upgaze; EEG is normal.

"opsoclonus-like" movements (Figure 1); rare vertical nystagmus was present in primary gaze. These episodes had a duration of 10 to 20 seconds each, appeared in small clusters, and were not accompanied by any clouding of consciousness; during the episodes the patient tried to look downward but was unable to gaze in that direction. Ten days previously, the boy had suffered from an upper respiratory viral infection. No other members of the family were affected. Neurologic examination, standard EEG, and video-EEG were normal. Ophthalmologic examination with fundus oculi and campimetry, metabolic investigations, cardiologic examination, electrocardiogram (ECG), catecholamine levels, abdominal ultrasonography, neuroradiologic (cerebral and medullary MRI) investigations, and karyotype were negative. Corticosteroid treatment was started on the basis of a virologic etiology, with partial resolution of the episodes.

At 3 years of age the boy suffered an episode of generalized hypertonia, lasting about 20 seconds, followed by sleep. Standard EEG revealed slight slow waves in the bilateral frontotemporal leads. Video-EEG, performed during tonic upgaze episodes, was normal. At present, tonic upgaze episodes have disappeared; neurologic examination reveals only a slight language disturbance.

Case 2

A boy aged 4 7/12 years was the only child of nonconsanguineous healthy parents. Pregnancy and delivery were uneventful. At 2 8/12 years he came to our attention because of sudden episodes of upward deviation of the eyes lasting a few seconds; these episodes were often associated with blinking and were not accompanied by any loss of consciousness (Figure 2); no nystagmus was observed in primary gaze. During the episodes, the patient was unable to look downward. No other members of the family were affected. Neurologic examination showed ataxia. Standard EEG, video-EEG, ophthalmologic examination with fundus oculi and campimetry, metabolic investigations, cardiologic examination, ECG, catecholamine levels, abdominal ultrasonography, neuroradiologic (cerebral and medullary MRI) investigations, and karyotype were negative. Benzodiazepine treatment was started on the basis of paroxysmal dystonia, with slowly progressive resolution of the episodes. At present, the boy is in good health; neurologic examination is normal.

Case 3

A girl aged 10 4/12 years was the first child of nonconsanguineous healthy parents. Pregnancy and delivery were uneventful. The girl come to our attention at the age of 9 8/12 years because of the sudden appearance of bouts of upward deviation of the eyes and drop-attack-like events lasting a few seconds, not coincidental with paroxysmal tonic upgaze. Paroxysmal tonic upgaze episodes

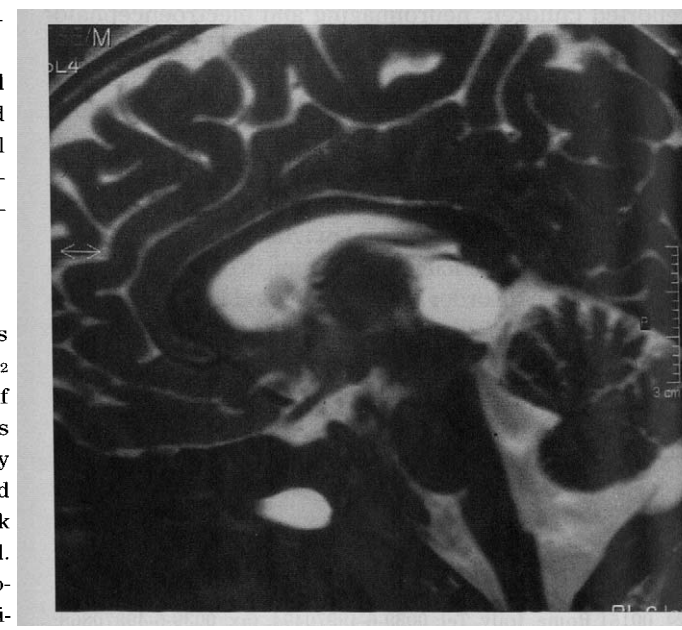

Figure 3. Pinealoma compressing the dorsal mesencephalon.

had a duration of 10 to 20 seconds each, appeared in small clusters, and were without any clouding of consciousness. No other members of the family were affected. Neurologic examination, ophthalmologic examination with fundus oculi and campimetry, metabolic investigations, cardiologic examination, ECG, catecholamine levels, abdominal ultrasonography, and karyotype were negative. Standard EEG revealed slow waves in the right parieto-occipital region with rare diffuse sharp waves. Anticonvulsant treatment was started, without modification of clinical manifestations. MRI revealed a pinealoma compressing the dorsal mesencephalon (Figure 3). After surgical removal of the pinealoma, the episodes of paroxysmal tonic upgaze and drop-attack-like events disappeared. At present, 1 year after surgical treatment, neither drop-attack-like episodes nor paroxysmal tonic upgaze are observed. Anticonvulsant drugs have been stopped; standard EEG is normal.

DISCUSSION

The vertical gaze is under the control of a complex network that includes the pretectal region in the dorsal mesencephalon, pons, and cerebral cortex.[12–14] Structural or functional pathologic conditions, lesional or "irritative," involving the dorsal mesencephalon can cause, respectively, paresis, paralysis, or paroxysmal upward deviation of the eyes, as demonstrated by experimental studies and clinical reports.[10,13,15,16] A central nervous system lesion of the gray matter of the dorsolateral periaqueductal region of the mesencephalon and the medial longitudinal fasciculus of the rostral interstitial nucleus can give rise to an upward tonic deviation of the eyes, usually associated with other neurologic signs.[8] Supranuclear structures involved in the control of conjugate eye motility are controlled by corticomesencephalic pathways originating in the prefrontal (area 8) and parieto-occipital cortices (areas 18 and 19).[12,13] Therefore, even involvement of these corticomesencephalic pathways can result in disorders of vertical gaze.

Paroxysmal tonic upgaze was reported originally by Ouvrier and Billson[1] as an oculomotor syndrome, possibly "benign," characterized by onset in infancy of periods of short conjugate upward deviation of the eyes without deterioration and with eventual improvement. This syndrome is usually classified as a "transient movement disorder in children".[17] In these infants neurologic examination, EEG, and metabolic and neuroradiologic investigations are normal.[1] Subsequently, the diagnosis has been extended to subjects affected by paroxysmal tonic upgaze with long-lasting episodes (from 30 minutes to 3 hours).[8] The association of neurologic and ophthalmologic disorders such as ataxia,[4,6,8–10] amblyopia and strabismus,[7] developmental delay,[10,11] and abnormal neuroradiologic features[2] has also been reported. Onset of paroxysmal tonic upgaze occurs either during or after an intercurrent infection or vaccination. Moreover, exacerbation of paroxysmal tonic upgaze with febrile illness is also reported.[1,6,11] Most therapeutic trials (eg, corticosteroids, drugs for intracranial hypertension, antiepileptic drugs, levodopa) have been performed with conflicting results.[6,9–11]

Paroxysmal tonic upgaze is not uncommon in the pediatric age. Differential diagnosis must be performed taking into account Kinsbourne syndrome, hidden neuroblastoma, myoclonic epilepsy, absence seizures, postencephalitic extrapyramidal syndromes, brainstem disorders causing downward gaze paresis such as mesencephalic tumors, alternating hemiplegia in childhood, pathologies with bilateral central visual loss secondary to retinal disease with preservation of the inferior visual field, intoxication, and the first stages of inherited neurometabolic diseases.[8–11,18]

Our three patients showed clinical characteristics consistent with the diagnosis of paroxysmal tonic upgaze, even if one of them was not completely representative of the syndrome described by Ouvrier and Billson in 1988. Patient 1 had, in association with paroxysmal tonic upgaze, language disabilities and ictal abnormalities seen on EEG in the frontotemporal regions, not correlated with paroxysmal tonic upgaze episodes as demonstrated by video-EEG, as also previously reported.[10] The coexistence in this case of other cortical problems (eg, speech delay) could sustain the hypothesis of corticomesencephalic pathway involvement. In patient 2, paroxysmal tonic upgaze represented the whole clinical picture with negative results in all investigations performed. Therefore, we can hypothize a functional involvement of the periaqueductal gray matter in the dorsal mesencephalon, probably on the basis of a transient immature function of neurotransmission, as suggested originally by Ouvrier and Billson in 1988. In patient 3, who was not very characteristic of the syndrome, a pinealoma compressing the dorsal mesencephalon, detected on MRI, probably caused the paroxysmal tonic upgaze and drop-attack-like events, since after surgical removal a complete resolution of the whole clinical picture was observed.

Our three patients could add new insight into the physiopathogenesis of paroxysmal tonic upgaze. It seems that any insult that involves periaqueductal mesencephalic gray matter could be considered a "conditio sine qua non" for the expression of this peculiar clinical manifestation. Paroxysmal tonic upgaze can still be considered a "benign" age-dependent pediatric neurologic condition. Nevertheless, a careful clinical, neurophysiologic, and neuroradiologic evaluation should be performed to detect possible structural lesions, mesencephalic in origin, causing paroxysmal tonic upgaze.

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