Benign paroxysmal torticollis in infancy: Report of two cases and aspects on pathogenesis

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ABSTRACT

Benign paroxysmal torticollis in infancy is characterized by periods of torticollis, usually occurring at the first year of life, at varying time intervals and typically resolves without complications within 1-5 years. It is thought to be a benign, self-limited paroxysmal disorder and has been regarded as a migraine equivalent, but the precise etiology remains unknown. We report two cases of recurrent episodes of torticollis and theories of etiology and pathophysiology are discussed including the potential role of mutations in the CACNA1A calcium channel.

Key words: benign paroxysmal torticollis, migraine equivalents, movement disorders

BACKGROUND

Benign paroxysmal torticollis in infancy (BPTI) was first described by Snyder in 1969.1 This condition is characterized by recurrent episodes of torticollis, sometimes followed by vomiting, pallor, ataxia, irritability or drowsiness, which resolve spontaneously within a few hours or days.

The pathogenesis of this disorder remains unknown. Some researchers regard BPTI as a migraine equivalent of infancy.2 It has also been reported that some patients with BPTI develop paroxysmal vertigo or migraine at an older age. Recent studies suggest that BPTI, benign paroxysmal vertigo and migraine are different phenotypic expressions of the same calcium channelopathy.3

We present two infants with recurrent episodes of BPTI and report the follow-up data to the outcome of the condition. We have also conducted a review of the literature on the pathogenesis of the disorder.

PRESENTATION OF TWO CASES

The first patient was an 8-month-old girl who was brought to the pediatric neurologic outpatient clinic due to recurrent episodes of torticollis from the age of 5 months. The episodes were usually noted upon awakening in the morning, alternated from side to side, lasted approximately 7 days and recurred after 7 days. The episodes resolved spontaneously with no residual deficit in the intervals. No other acute symptoms were associated with the paroxysmal torticollis in this case.

The infant was the second child of apparently healthy parents. The father of the infant suffered from recurrent episodes of headaches, not further investigated. The patient had a healthy 2-year-old sister. She was born after an uncomplicated pregnancy (planned cesarean section), with a birth weight of 2850 g. The patient had a normal physical and psychomotor development. She had received all the doses of the routine childhood immunization schedule for her age. Serious medical problems or use of medications were not reported in the infant’s history. Symptoms of gastroesophageal reflux were not noted.

Painless torticollis on the right side was diagnosed on physical examination. The standardized neurologic evaluation and the rest unremarkable physical findings did not support the diagnosis of a neurologic deficit.

The precise choice of laboratory tests required for an evaluation of paroxysmal torticollis has not been standardized but can be seen as two sets. In the first set are those studies needed for evaluation of secondary disorders that could mimic a BPTI. These studies include a complete blood count, erythrocyte sedimentation rate (ESR), screening chemistries of liver and kidney function, and blood glucose levels, as well as C-reactive protein (CRP).

Laboratory investigation revealed the following results: WBC count 17000 /ml with a predominance of lymphocytes, Hb(Hemoglobin) 11.7 g/dl, Ht 35%, ESR 11 mm/1h, CRP 3.5 mg/L and normal biochemical profile. The second area of laboratory testing relates to the detection of associated disorders. Orthopedic abnormalities were excluded with conventional radiography of the cervical spine. Ultrasonography of the brain and neck were also performed, with normal findings. The sonographic appearance of the gastroesophageal junction and the 24-hours pH monitoring of the oesophagus did not indicate the presence of gastroesophageal reflux. MRI of the brain and EEG(electroencephalogram) as well as the detailed ophthalmologic and ENT (Otolaryngologic) tests within physiologic patterns.

The infant was followed-up until 13 months of age and continued to have recurrent episodes of torticollis with the same clinical characteristics and without the development of secondary symptoms or/and physical findings.

The second case involves an 8-month-old girl who presenting with torticollis, pallor, localized cyanosis around the mouth lasting for a few seconds only-vomiting and drowsiness. Three previous episodes of paroxysmal torticollis were noted in her history, which had resolved after paracetamol administration, according to the parents. No residual abnormality was observed during the intervals.

The infant was the first child of apparently healthy parents. She was born by cesarean section at the 38th week of

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gestation. During the pregnancy, her mother had a pathological oral glucose tolerance test. She reportedly had an unremarkable past medical history with normal development. She had received all her immunizations and had a negative family history.

On physical examination, the infant presented with torticollis on the right side, but was otherwise normally active, with no other symptoms. The standardized neurologic evaluation showed a mild hypotonia of the trunk, while the rest of physical findings were completely normal.

The WBC count was 14000/mm³ with a predominance of lymphocytes, Hb 10.2 g/dl, Ht 31.9%, ESR 20 mm/1h, CPK 252 U/L, while the biochemical and routine metabolism tests were normal. The fall eye examination and the EEG were normal. The imaging of the brain and the cervical spine with conventional radiography and MRI did not demonstrate any pathologic findings. PH monitoring of the esophagus showed a mild gastroesophageal reflux, which was treated with domperidone and omeprazole. We decided to recommend this treatment in case the diagnosed gastroesophageal reflux was the reason for torticollis (such as in Sandifer syndrome). The ultrasound of the heart, excluded congenital heart diseases that might contribute to the localized cyanosis around the mouth, vomiting and drowsiness.

The infant continued to have rare episodes of torticollis, with the same clinical features, up to the age of 3 years. At present, the child is 4 years old and has been free of symptoms for the past 12 months.

Based on the history, clinical examination, laboratory investigation and follow-up, both infants were diagnosed as suffering from benign paroxysmal torticollis of infancy.

**CONCLUSION AND REVIEW OF THE LITERATURE**

The first report of recurrent episodes of torticollis, presenting in infancy and resolving after the age of five years, was made in 1969 by Snyder, who studied 12 children. In the following years, there were many reports of children with this paroxysmal disorder and, until now there are about 80 cases reported in the literature. In all cases of BPTI, the clinical course has the same pattern: a) the episodes of torticollis typically begin at the first months of life, b) they recur with varying intervals, usually from 2 to 45 days, but the frequency and intensity decrease with age, c) the duration of those effects varies from a few minutes to 15 days and d) they resolve spontaneously after the age of 1 to 5 years.

Thus, during the first episode of torticollis we must exclude a posterior fossa tumor. Major causes of paroxysmal torticollis include benign paroxysmal torticollis, spasmodic torticollis and dystonia, spasms nutans, Sandifer's syndrome, familial paroxysmal torticollis, tics and Tourette's syndrome. Sandifer's syndrome is a rare manifestation of gastroesophageal reflux in children that occurs in association with abnormal movements and postures of the head, neck, and trunk. The differential diagnosis also includes congenital malformations of the cervical spine, such as atlanto-occipital fusion and congenital cervical scoliosis, visual disturbances and dystonic drug reactions. In some cases, torticollis may be a sign of a serious underlying process. MRI imaging of the brain may be necessary in order to rule out a space occupying lesion in the posterior fossa. Yasumoto et al reported a case of an infant that presented with BPTI at the age of 8 months and at the age of 3 months with hemiplegia. The investigation revealed that the underlying disease was Moya-Moya syndrome. Epilepsy has been considered in the differential diagnosis, but there is not relevant evidence.

The pathogenesis of BPTI is not clear. Snyder (1969) suggested that the underlying cause is a peripheral vestibular disorder, such as labyrinthitis. However, this approach was questioned in the following years. Sanner and Bergstrom (1979) regarded BPTI rather as a vascular or metabolic disorder, due to its paroxysmal nature. According to the latter, epilepsy is not related to the episodes of torticollis, as the EEG tests during the paroxysms were normal in their study.

Deonna and Martin questioned, as well, Snyder's remarks and considered a central impairment of the vestibular system and the vestibulocerebellar connections, among the existing etiolo-

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**Table 1. The full spectrum of clinical manifestations and epidemiological data of BPTI in selected studies.**

<table>
<thead>
<tr>
<th>Category</th>
<th>Veksler</th>
<th>Cohen</th>
<th>Chutorian</th>
<th>Deonna</th>
<th>Drigo</th>
<th>Giffin</th>
<th>Hamakoglo</th>
<th>Santer</th>
<th>Snyder</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Female</strong></td>
<td>1</td>
<td>4</td>
<td>3</td>
<td>10</td>
<td>1</td>
<td>3</td>
<td>4</td>
<td>4</td>
<td>1</td>
<td>64</td>
</tr>
<tr>
<td><strong>Age of onset</strong></td>
<td>3 months</td>
<td>2-8 months</td>
<td>*</td>
<td>2 months</td>
<td>*-1 year</td>
<td>1-8 months</td>
<td>3-6 months</td>
<td>7 months</td>
<td>1 week</td>
<td>2 months</td>
</tr>
<tr>
<td><strong>Duration</strong></td>
<td>24 hours</td>
<td>4 hours</td>
<td>Hours</td>
<td>1 hour</td>
<td>Minutes</td>
<td>10 minutes</td>
<td>5 hours</td>
<td>3 hours</td>
<td>14 days</td>
<td>14 days</td>
</tr>
<tr>
<td><strong>Age of recovery</strong></td>
<td>9 months</td>
<td>2-5 years</td>
<td>2-3 years</td>
<td>2-5-3 years</td>
<td>&lt;3 years</td>
<td>3-4 years</td>
<td>1-1-3 years</td>
<td>10 months</td>
<td>5 years</td>
<td>3 months</td>
</tr>
<tr>
<td><strong>Development of migraine or other periodic syndrome</strong></td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>*</td>
</tr>
<tr>
<td><strong>Family history of BPTI</strong></td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>*</td>
</tr>
<tr>
<td><strong>Family history of migrants</strong></td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>*</td>
</tr>
<tr>
<td><strong>Family history of epilepsy</strong></td>
<td>*</td>
<td>*</td>
<td>*</td>
<td>12</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>*</td>
</tr>
</tbody>
</table>

*No evidence given by the authors.*
gy theories. They also observed that in some cases there was an increased familial incidence of BPTI in migraines, as well as development of secondary migraine at an older age. Based on these observations they came into the conclusion that BPTI is, at least in some cases, a migraine equivalent that is attributed to a transient disorder of vascularisation of the CNS from the basilar artery.

Kimura and Nezu (1998) reported that the electromyography (EMG) of the sternocleidomastoid muscle during the episode of torticolis showed continuous electrical discharges in one case. They suggested that BPTI is a dystonic disorder and should be categorized as "idiopathic paroxysmal dystonia in infancy", and not as "torsion dystonia", which has the same findings in EMG, but different clinical features.

Drigo and his colleagues (2000) studied 22 patients with BPTI, the biggest series of patients studied until today. In this study 54.5% of the patients had a positive family history of migraine, 35.5% presented with migraine or a migraine equivalent after the BPTI resolution and 34.5% had a positive family history of traveler's disease (kinetosis). The last observation is not referred in other studies. The authors note that the predominant presence of (kinetosis) in BPTI patients indicates the probability of a vestibular impairment in BPTI pathophysiolo.

Moreover, the correlation between BPTI and migraine is a challenge for investigators in cases with positive for migraine family history.

Giffin and his colleagues (2002) reported 4 new cases of BPTI. In all cases, after the episodes of torticolis were resolved, they were replaced by paroxysmal vertigo or migraine headaches and in all cases there was a family history of migraine with ataxia. Gene analysis in 2 cases revealed a mutation in the gene that encodes the Ca\textsuperscript{2+}1aI pore forming subunit of Ca++ channels (CACA\textsuperscript{1A}) in the chromosome 19p13. Mutations in the same gene have been found in cases of familial hemiplegic migraine by other researchers, while mutations have also been reported for genes of chromosome 1q21-23 and 1q32.

Aiming to the interpretation of the current research data, Giffin and his colleagues established the hypothesis that this Ca++ channelopathy is responsible for the cervical dystonia, based on the CACA\textsuperscript{1A} mutation combined with the EMG results in the Kimura and Nezu study. The cerebellum could possibly play a key role for the development of dystonia and this suggestion is also compatible with the CACA\textsuperscript{1A} mutation theory. It has been found that the CACA\textsuperscript{1A} gene is expressed in the cortex of the cerebellum. An automatic change in the level of the Ca++ channels activation is responsible for the episodic pattern of the disorder. The same authors try to explain the mechanism through which a mutation can be responsible for varying manifestations in different stages of development. The expression of CACA\textsuperscript{1A} may be regulated by other genes (especially for the \(\beta\) and \(\gamma\) subgroup of CACA\textsuperscript{1A}) which may be activated in different stages of development by biochemical/ hormonal changes, like the cyclic hormonal profile in the beginning of menstruation.\textsuperscript{1,2} It has been suggested by many authors that the BPTI should be considered as a pediatric migraine equivalent (International Headache Society-IHS).\textsuperscript{2,4} The current IHS classification includes only abdominal migraine, cyclic vomiting and benign paroxysmal vertigo of childhood as migraine equivalents (Headache Classification Committee, 2004). BPTI fulfills all criteria established by IHS: full recovery between the episodes, family history of a migraine syndrome or migraine, clinical manifest-

<table>
<thead>
<tr>
<th>Table 2: The main characteristics of BPTI and their Incidence. The conducted search included medline and scopus databases and provided 61 reported cases of international bibliography. Selected papers are found in 1-13 references.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Characteristics of BPTI</strong></td>
</tr>
<tr>
<td>Female sex</td>
</tr>
<tr>
<td>Presence of accompanying symptoms</td>
</tr>
<tr>
<td>Onset of symptoms in the morning hours</td>
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<tr>
<td>Triggerring factors</td>
</tr>
<tr>
<td>Development of migraine or other migrainous syndromes</td>
</tr>
<tr>
<td>Family history of BPTI</td>
</tr>
<tr>
<td>Family history of migraine</td>
</tr>
<tr>
<td>Family history of traveler's disease</td>
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<tr>
<td>Abnormal posture of the trunk</td>
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</tbody>
</table>

In conclusion, review of the literature indicates that a genetic disorder in the calcium channels may cause BPTI. The theory that BPTI may be a migraine equivalent is still vital and fully combatible with current research data from genetics and molecular biologists. It is a wise policy for clinicians to avoid unnecessary tests and therapeutic agents in BPTI. However, long term follow-up of the child is advised for the development of secondary symptoms.

REFERENCES