Chiari I malformation manifesting as bilateral trigeminal neuralgia: case report and review of the literature

INTRODUCTION

Trigeminal neuralgia (TN) is characterised by recurrent episodes of sudden, intense, usually unilateral, lancinating pain confined to the distribution of one or more branches of the trigeminal nerve. It is most commonly associated with compression of the trigeminal nerve root by an artery or vein, which is thought to lead to irritability of the nerve root due to demyelination and remyelination at the root entry zone. However, some cases are associated with central lesions such as multiple sclerosis, tumours, arteriovenous malformations and brainstem infarcts. There are also several case reports of unilateral TN in the setting of Chiari I malformation, where decompression of the posterior fossa or shunting procedures for associated hydrocephalus have led to relief from TN symptoms.1–5 We present the first reported case of bilateral TN as the sole manifestation of Chiari I malformation. Unlike previous cases where unilateral TN was accompanied by other Chiari malformation symptoms, bilateral TN was the sole manifestation of this patient’s Chiari I malformation.

CASE REPORT

A 56-year-old woman with a 5-year history of left-sided TN presented to the emergency room with the chief complaint of intermittent, sharp, burning discomfort along the V3 distribution on the right side of her face over the previous 3 weeks. The pain began after an episode of severe coughing and was described as a burning, electrical-type pain radiating from the periauricular area to below the lip on the right side of her face. The pain typically lasted 5–10 s, but occasionally as long as 20–30 s. It was trigeminal in origin with the chief complaint of intermittent, sharp, burning discomfort along the V3 distribution on the right side of her face. While eating or chewing, the pain was triggered by eating crunchy or cold foods, drinking hot liquids and brushing her teeth. Medical management with oxcarbazepine and carbamazepine was attempted without success, as she continued to experience pain on 5–10 daily pain episodes.

The patient’s past medical history was notable for left-sided TN (well-controlled with oxcarbazepine and baclofen), hypertension and gastro-oesophageal reflux disease. Medications included oxcarbazepine, carbamazepine, acetaminophen/hydrocodone, clonidine, carvedilol, hydrochlorothiazide, omeprazole and conjugated estrogen. The patient’s neurological examination revealed no focal deficits. She had no dysmetria, ataxia, nystagmus, hyper-reflexia or loss of facial sensation. Given that she had never had any imaging performed, MRI of brain and cervical spine with and without gadolinium was obtained and revealed downward displacement of the cerebellar tonsils 2 cm below foramen magnum along with a cervical syrinx, consistent with a radiographic diagnosis of Chiari I malformation (figure 1). There was also evidence of impaired CSF flow posteriorly along the brainstem as evident on MRI cine flow study; however, there was no evidence of hydrocephalus.

The patient underwent suboccipital craniectomy with cervical laminectomy for decompression of Chiari I malformation without complications. She was discharged on postoperative day 5 without any facial pain. Incisional pain was managed with oral narcotics (hydrocodone/acetaminophen), and she was maintained on oxcarbazepine for neuralgia. Her oxcarbazepine dose was reduced to 600 mg twice daily compared with 1550 mg twice daily prior to surgery. At several follow-up visits over a 9-month period, the patient had no facial pain, and facial sensation and activation were intact bilaterally.

DISCUSSION

TN can be categorised as primary or secondary according to its underlying cause. Primary TN results from vascular compression of sensory root entry zone. Secondary TN, however, is associated with a wide range of conditions, including multiple sclerosis, aneurysms, arteriovenous malformations and posterior fossa mass lesions. Carbamazepine is the first-line treatment for TN that is not caused by an obvious structural lesion, with an approximate 70% patient response rate. Indications for surgery in TN include refractory to medical therapy, as well as symptoms secondary to an accessible mass lesion.

In the English literature, there are 20 previously reported cases of unilateral TN associated with Chiari I malformation.1–4 Treatment by suboccipital craniectomy with or without laminectomies, duraplasty or tonsillar aspiration was performed in 15 of these 20 patients, with complete resolution of pain in 11 patients (75%). Two other patients (15%) became pain-free after undergoing additional microvascular decompression, and the two remaining patients experienced improved but residual pain. Of the five patients who did not undergo surgical decompression by suboccipital craniectomy, two had hydrocephalus, one underwent third ventriculopontine shunting, and the other underwent third ventriculostomy, both with complete resolution of symptoms. Another patient became pain-free while maintained on carbamazepine treatment. Data for the remaining two patients are unavailable.

The precise mechanism by which Chiari I malformation leads to TN is not clearly understood, although several hypotheses have been entertained. First, extra-axial elongation of the trigeminal nerve root secondary to brainstem displacement (such as with basilar invagination) could lead to demyelination and remyelination in trigeminal sensory fibres and formation of artificial synapses, leading to symptoms of TN.2 Another hypothesis is that compression of the spinal trigeminal pathway by cerebellar tonsillar herniation could lead to TN. The spinal nucleus, the first relay of trigeminal fibres sensitive for pain in the spinal trigeminal pathway, extends from pontomedullary junction to C2 segment of the spinal cord, and compression of this pathway by cerebellar tonsillar herniation as well as cervical spinal syrinx could cause TN.4 Improvement in symptoms upon decompression of posterior fossa leads further support to this hypothesis.2,4 Third, it has been proposed that the presence of a cervical syrinx may contribute to TN symptoms. The presence of a cervical syrinx may indirectly result in vascular compression or stretching of trigeminal nerve at nerve root entry zone. The presence of a syrinx may damage sensory fibres arising from trigeminal nucleus and impact excitability as they descend down to C2 before coursing rostrally and exiting the brainstem. Others reported that treatment of hydrocephalus associated with Chiari I malformation can lead to resolution of TN symptoms.1 Since hydrocephalus outside the context of Chiari I malformation has not been associated with TN, rationale for pain resolution in shunted Chiari I patients must entail a decreased pressure gradient with less compression from cerebellar tonsils. While several mechanisms and surgical approaches seem successful in treating medically refractory TN patients, it is important to recognise Chiari I malformation as a possible treatable cause of TN.

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abnormalities on MRI dystonia and basal ganglia with early onset generalised mutations in Brazilian patients


REFERENCES

Low prevalence of PANK2 mutations in Brazilian patients with early onset generalised dystonia and basal ganglia abnormalities on MRI

Neurodegeneration with brain iron accumulation (NBIA) is a heterogenous group of degenerative diseases presenting with movement disorders. Causative mutations have been identified, first in PANK2, encoding pantothenate kinase 2, and later in PLA2G6, a calcium independent phospholipase A2 enzyme.1,2 NBIA types 1 and 2 are the denominations used to label these two entities. The clinical picture includes pyramidal syndrome, movement disorders, cerebellar dysfunction, ophthalmoplegia and oculumotor disturbance. A neuroradiological hallmark of NBIA type 1 is the “eye-of-the-tiger” sign, characterised by bilateral areas of hyperintensity surrounded by a ring of hypointensity in the medial globus pallidus on T2-weighted MRI. Radiological findings in NBIA type 2 comprise cortical atrophy in the cerebellum, increased iron deposition in globus pallidus and substantia nigra seen as reduced signal on T2 FLAIR and T2 gradient and diffusion weighted MRI sequences, reduced volume of the optic chiasm and optic nerves and cerebral white matter changes. In this paper, we report clinical, neurological and molecular findings of Brazilian patients with clinical diagnosis of NBIA type 1.

METHODS
We identified consecutive patients during the years of 2005 and 2006 in the UFMG Movement Disorders Clinic with early onset generalised dystonia and basal ganglia abnormalities on neuroimaging studies compatible with the diagnosis of NBIA. We performed a detailed family history assessment and neurological exam and rated dystonia with the Burke—Fahn—Marsden Scale. DNA was extracted from peripheral lymphocytes according to routine procedures. Amplification of the coding exons of PANK2 by polymerase chain reaction was performed as previously described, followed by sequencing.1 The study was approved by the local ethics committee and recruited patients provided signed informed consent.

RESULTS
We examined 576 patients, of whom 195 had a diagnosis of dystonia. From the dystonia group, 14% had early onset (age at onset—14.8 (7.7) years) and 6 (3% of all dystonia patients) displayed imaging changes in the basal ganglia consistent with those seen in NBIA type 1: five had the typical “eye-of-the-tiger” sign and one had a reduction in T2 signal in the globus pallidi and substantia nigra (Table 1). Blood count, liver and kidney function, lipid profile, alpha-fetoprotein, serum B12, folate, copper, ceruloplasmin, ferritin, serum immunoglobulin, creatinine phosphokinase, serum lactate and ammonia were normal in all patients submitted to this study. The age at onset of NBIA was 15.8 (10.5) years. Sequence analysis revealed that three brothers had a homozygous mutation (N294I) of the PANK2 gene. These patients, born of a consanguineous marriage, had onset of their illness at the age of 16, 26 and 30 years, presenting with focal dystonia (writer’s cramp), paroxysmal dystonia, epilepsy, Parkinsonism (hypophonia, bradykinesia, postural instability, festination and gait freezing), dysarthria, pyramidal signs and the “eye-of-the-tiger” sign on MRI. The illness of all patients has displayed a slow progression. The Burke—Fahn—Marsden Scale scores of the patients were, respectively, 7, 14 and 10 and did not change over time. There was no response to therapeutic agents such as levodopa and biperiden. Sequence analysis of the PANK2 gene of the other three patients, two with the typical “eye-of-the-tiger” sign, did not reveal mutations in PANK2.

Table 1 Clinical description of the patients

<table>
<thead>
<tr>
<th>Patient</th>
<th>Gender</th>
<th>Age at onset</th>
<th>Familial history</th>
<th>Consanguinity</th>
<th>First symptom</th>
<th>Features</th>
<th>Image</th>
<th>PANK2 mutations</th>
</tr>
</thead>
<tbody>
<tr>
<td>200656</td>
<td>M</td>
<td>2</td>
<td>Negative</td>
<td>Negative</td>
<td>Gait disturbance (equinovarus foot)</td>
<td>Anarthria, generalised dystonia, opisthotonus, Babinski sign</td>
<td>Reduction in T2 signal in the globus pallidi and substantia nigra</td>
<td>Negative</td>
</tr>
<tr>
<td>200666</td>
<td>F</td>
<td>12</td>
<td>Negative</td>
<td>Negative</td>
<td>Gait disturbance and dystonia</td>
<td>Ataxia, cognitive impairment, generalised dystonia, ophthalmoplegia, anarthria and dysphagia</td>
<td>Eye-of-the-tiger sign</td>
<td>Negative</td>
</tr>
<tr>
<td>200635</td>
<td>F</td>
<td>9</td>
<td>Negative</td>
<td>Negative</td>
<td>Gait disturbance and dystonia</td>
<td>Spasticity, aquiluone clonus, Babinski sign, rigidity, generalised dystonia</td>
<td>Eye-of-the-tiger sign</td>
<td>Negative</td>
</tr>
<tr>
<td>200642*</td>
<td>M</td>
<td>30</td>
<td>Positive, sister and brother</td>
<td>Positive</td>
<td>Writer cramp</td>
<td>Hyperreflexia, slight isometric and intentional tremor, dysarthria, hypophonia, postural instability and bradykinesia</td>
<td>Eye-of-the-tiger sign</td>
<td>N294I</td>
</tr>
<tr>
<td>200641*</td>
<td>F</td>
<td>16</td>
<td>Positive, two brothers</td>
<td>Positive</td>
<td>Dyssartria and Gait disturbance</td>
<td>Epilepsy, rigidity, bradykinesia, postural tremor, enhanced reflexes, disinnery, postural instability, paroxysmal dystonia, freezing and gait festination</td>
<td>Eye-of-the-tiger sign</td>
<td>N294I</td>
</tr>
<tr>
<td>200643*</td>
<td>M</td>
<td>26</td>
<td>Positive, sister and brother</td>
<td>Positive</td>
<td>Isometric and postural tremor in superior limbs</td>
<td>Retropulsion, dysarthria, mask face, bradykinesia, clonus, Babinski sign</td>
<td>Eye-of-the-tiger sign</td>
<td>N294I</td>
</tr>
</tbody>
</table>

*Siblings.