

# INFLUENCE OF LAMOTRIGINE OVER THE SUNCT SYNDROME

## ONE PATIENT FOLLOW-UP FOR TWO YEARS

### Case report

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**ABSTRACT** - The SUNCT syndrome is characterized by a short-lasting headache in the first division of the trigeminal nerve, associated with ipsilateral autonomic symptoms. It is highly refractory to prophylactic medication. We describe a case where lamotrigine reduced the intensity, duration, and frequency of attacks and increased the remission period of this disorder. Over a two-year period, the attacks came back immediately whenever the patient reduced the dose or neglected treatment. We concluded that lamotrigine is effective in treating SUNCT syndrome when used in high doses for a prolonged period of time.

**KEY WORDS:** lamotrigine, prophylactic treatment, SUNCT syndrome, trigeminal autonomic cephalalgia.

#### **Influência da lamotrigina sobre a síndrome SUNCT: comportamento de um paciente durante período de dois anos**

**RESUMO** - A síndrome SUNCT caracteriza-se por cefaléia de curta duração localizada na primeira divisão do nervo trigêmeo e associada com sintomas autonômicos ipsilaterais. A resposta clínica aos diversos tratamentos profiláticos propostos têm sido caracterizados pela alta refratoriedade. Nós descrevemos um caso em que a lamotrigina reduziu a intensidade, duração e frequência dos ataques, aumentando o período de remissão. Por um período de dois anos em que utilizamos a lamotrigina, surgiram novos ataques quando o paciente reduziu a dose ou negligenciou o seu tratamento. Concluímos que lamotrigina é tratamento eficaz para a síndrome SUNCT quando utilizada em altas doses e por período prolongado de tempo.

**PALAVRAS-CHAVE:** cefaléias trigemino-autonômicas, lamotrigina, SUNCT síndrome, tratamento profilático.

Shortlasting, unilateral, neuralgiform headache with conjunctival injection and tearing (SUNCT syndrome) was first described by Sjaastad 25 years ago<sup>1</sup>. During this period, some new clinical evidences were included in the spectrum of this syndrome, but our knowledge of this disorder is constantly advancing.

We describe a case responsive to lamotrigine and review the current literature on SUNCT.

#### **CASE**

A 45-year-old man had a five-year history of severe shooting pain over the left eye that lasted 30 seconds and occurred as often as 20 times a day. These symptoms were accompanied by intense ipsilateral tearing, conjunctival

injection, and nasal congestion. Attacks could be provoked by touching the left temporal region, putting his foot on the ground, eating, or moving his neck. General physical and neurologic examinations, routine blood analysis, and CT and MRI of the brain were normal. The patient tried indomethacin 200mg/day, verapamil 480mg/day, carbamazepine 1200mg/day, phenytoin 300mg/day, valproate 1000mg/day, and greater occipital and supraorbital blocker with bupivacaine and steroids, all without effect. During the attacks, he used oxygen and triptans but had poor results. The patient also had thermocoagulation of the ipsilateral trigeminal ganglion performed. He had a good result and was symptom-free for two years, but the attacks then returned. Methysergide 4mg/day and celecoxib 300mg/day partially relieved the headache but these me-

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dications had to be discontinued as the patient showed significant side effects. The patient was subsequently tried on lamotrigine, with the dose being increased by 50mg every 10 days until a total dose of 300mg/day was reached. There was continued improvement. He had no new headaches for five months, at which time the lamotrigine was tapered to 100mg/day and the attacks returned at the rate of 10 attacks per day. Lamotrigine was increased to 300mg/day and the attacks were eliminated after 45 days. On one occasion, the patient neglected to take his medication for one week. The attacks returned and only disappeared 30 days after reintroducing the medication. We have followed this patient for more than eight months. He has been on adequate dose of lamotrigine and has had no new attacks.

## DISCUSSION

SUNCT syndrome is one of a number of trigeminal autonomic cephalalgias characterized by short-lasting headache occurring in the first division of the trigeminal nerve<sup>2,3</sup>. The pain is maximal in and around the eye and may radiate to the ipsilateral forehead, temple, nose, cheek, and palate<sup>4</sup>. Attacks are typically unilateral, although in some cases the pain also simultaneously occurred on the opposite side<sup>4</sup>. The pain is usually burning, stabbing, or electrical in nature<sup>4</sup>. The paroxysms begin and end abruptly, reaching maximum intensity within 2 to 3 seconds<sup>4</sup>. The pattern of solitary attacks is usually "plateau-like" but other patterns, such as "repetitive", "saw-toothlike", and "plateau-like plus exacerbations" have been noted<sup>5</sup>. Individual headache attacks last between 5 and 250 seconds each (mean 49 seconds)<sup>6</sup>; attacks lasting 2 hours have also been described<sup>7</sup>. A dull interictal discomfort may or may not persist between acute episodes<sup>7,8</sup>. Four patients experienced a "status-like" pattern, in which painful paroxysms persisted for 1 to 3 days<sup>9</sup>.

The temporal pattern is also quite variable, with symptomatic periods alternating with periods of pain-free remissions in an erratic fashion. Symptomatic periods generally last from a few days to several months and occur once or twice yearly. Remissions range from 1 week to 7 years but usually are of several months' duration<sup>4,7</sup>. A bimodal distribution with increased attack frequency occurring in the morning and afternoon/evening hours has been described<sup>6</sup>, and nocturnal attacks can occur<sup>4</sup>. During symptomatic phases, attacks may be precipitated by a variety of triggers located within trigeminal and/or extra-trigeminal areas. Precipitants include touching the hair, forehead, face, nose, and lip on the symptomatic side. Washing, shaving, eating, chewing,

tooth-brushing, talking, and coughing were also reported as headache triggers<sup>4</sup>. Mechanical movements of the neck can also precipitate attacks, and in some cases abort them<sup>2,4</sup>. Our patient related that his paroxysms were triggered when he touched his foot over the ground, touched the temporal region, ate, or moved his neck.

The acute attacks are accompanied by ipsilateral conjunctival injection, lacrimation, nasal congestion, rhinorrhea, and eyelid edema<sup>8</sup>. In some patients, autonomic symptoms were bilateral, although more pronounced on the side of the headache<sup>4</sup>. The associated tearing and conjunctival injection usually begins 1 to 2 seconds following the acute episodes of pain and may persist for a few seconds longer than the painful episodes<sup>4</sup>. The symptoms can remain 30 to 60 seconds following headache resolution<sup>2,10</sup>, and in rare cases until 10 minutes post resolution<sup>11</sup>.

Most cases occur in men<sup>4</sup> (male:female ratio 17:2)<sup>5</sup>; the age of onset ranges from 23 to 77 years (mean 51 years)<sup>4</sup>. The etiology is unknown, but recently cases secondary to cerebellopontine angle arteriovenous malformations<sup>12,13</sup>, brain stem cavernous hemangioma<sup>14</sup>, a posterior fossa lesion in a patient with AIDS<sup>3</sup>, prolactinomas<sup>15</sup>, and corneal lesion<sup>16</sup> have been described.

Excluding symptomatic cases, CT, MRI, and angiography, when performed, were essentially normal. In some cases, orbital phlebography reveals a narrowed superior ophthalmic vein ipsilateral to the headache<sup>17</sup>. Ipsilateral Intraocular pressure and corneal temperatures are increased, as is forehead sweating, during attacks<sup>17,18</sup>, but pupillometry and pharmacologic studies of the pupil are normal<sup>19</sup>. Single photon emission computed tomography and transcranial doppler studies are normal during attacks<sup>20,21</sup>. One patient with SUNCT syndrome had activation in the posterior hypothalamic grey on functional MRI during one attack<sup>22</sup>. These findings demonstrate for the first time that a central nervous system dysfunction may be involved in the pathophysiology of SUNCT.

SUNCT syndrome is, perhaps, the most refractory of all primary headache disorders. Rare cases are responsive to gabapentin<sup>23-25</sup>, topiramate<sup>26</sup>, carbamazepine<sup>4</sup>, corticosteroids, or surgical procedures<sup>27</sup>. Some cases did not improve after surgical treatment, and there was significant morbidity<sup>28</sup>. Verapamil and omeprazole were reported to worsen the headache<sup>29</sup>. Nonsteroidal anti-inflammatory drugs and tricyclic antidepressants showed minimal effect<sup>29</sup>. Lamotri-

gine, a new antiepileptic drug used for treating other painful neurologic syndromes<sup>30-32</sup>, has shown good results in the treatment of SUNCT syndrome<sup>33-37</sup>. Lamotrigine acts by stabilizing the neuronal sodium channel<sup>38</sup>, which suppress the excessive release of glutamate. As a potent antiglutamatergic drug, it is involved in the N-methyl-D-aspartic acid neurotransmitter, which acts on the antinociceptive pathway responsible for the establishment of chronic pain<sup>39</sup>. Lamotrigine also reduced pain behavior in a rat model of neuropathic pain<sup>40-41</sup>.

By beginning with low doses and gradually increasing, side effects such as skin rash can be avoided (there is a case report of a fatal outcome with this skin rash)<sup>42</sup>. Lunardi et al report that when lamotrigine is used in trigeminal neuralgia there is a direct relationship between daily dose, plasma level of lamotrigine, and analgesic effect; this study shows that pain relief is proportional to the daily dosage and to drug plasma levels, with the maximum daily dosage used being 400mg<sup>43</sup>. This effect on the SUNCT syndrome was observed in our case and in the recent papers<sup>37</sup>.

In our case, the temporal pattern changed after the patient was started on lamotrigine. The initial dose of 100mg reduced the number of SUNCT attacks from 30 per day to 10 per day. When we increased the dose to 300mg/day (100mg tid), the attacks progressively reduced until they finally disappeared. After this initial response, the patient relapsed on three occasions: once because he neglected to take the medication and twice because he reduced the dose. After reintroducing the medicine, the attacks continued for two more weeks, reducing progressively in the next two weeks until they disappeared. During these periods, the patient used different analgesics, triptans, NSAIDs, codeine and corticosteroids with poor results. A block of the greater occipital and supraorbital nerves with corticosteroids and bupivacaine was also futile.

Here we see the influence of lamotrigine on the behavior of the attacks and probably over the cyclical pattern. The etiology of SUNCT syndrome may be related to the posterior hypothalamic grey<sup>22</sup>, thereby explaining its cyclical behavior. Lamotrigine improved the headache and induced a change in the cyclical behavior. During lamotrigine reintroduction, the pain did not abate, which showed us that the subsequent action of the drug is more gradual.

Our patient that has used lamotrigine for two years, and it has reduced the intensity, duration and

frequency of the SUNCT attacks, and has kept the patient asymptomatic for a longer time. To induce a remission, the patient required a high dose of lamotrigine (300mg/day) and treatment of at least 2 weeks or more.

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