CASE REPORT

SUNCT Syndrome Successfully Treated with the Combination of Oxcarbazepine and Gabapentin

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ABSTRACT

Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) is a syndrome of intermittent, brief, unilateral, severe paroxysms of orbital-temporal pain recurring multiple times per day. The pain modulation is often very difficult. The reported SUNCT patient is the first who responded to a combination treatment of oxcarbazepine and gabapentin.

Key Words. SUNCT; Oxcarbazepine; Gabapentin

Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) is a syndrome of intermittent, brief, unilateral, severe paroxysms of orbital-temporal pain recurring multiple times per day [1]. The incidence is very low, up to now only about 200 cases worldwide have been reported. Pain intensity is moderate to severe; the character is burning, stabbing, or lancinating, lasting from 5 to 240 seconds. The frequency of the pain attacks can range from one to two crises per day to 10–30 crises per hour [2,3]. SUNCT syndrome is refractory to a variety of therapeutic approaches; only antiepileptic drugs and lidocaine and phenytoin intravenously seem to modulate the pain [4–8].

We report the first SUNCT patient who has successfully been treated with the combination of oxcarbazepine and gabapentin.

Case Report

A 65-year-old man was referred to our out-patient clinic with a 2-month history of unilateral cephalalgia. The headache was described as stabbing periorbital pain, localized to the area of the right cheek and temple and radiating to the right lower jaw to a lesser extent. The pain could be triggered by chewing, touching, and speaking. Occasionally, lacrimation of the right eye accompanied the attacks. Two weeks before a trigeminal neuralgia was diagnosed and a therapy with slow releasing carbamazepine was started. Piritramide, morphine, and nonsteroidal anti-inflammatory drugs (NSAIDs) and oxygen in the acute attack were ineffective. Carbamazepine (800 mg) and benperidol (15 mg) in combination resulted in a temporary relief of the complaints, but the pain exacerbated in intensity and frequency 2 weeks later under the medication.

At admission, he complained of severe lancinating pain, thrusting, and burning in character, a headache with a level 9 out of 10 of the visual analog scale. By touching the right periorbital region, combing the hair, and taking a shower attacks could be induced. A ptosis and chemosis of the right eye was noticed. During the attacks, which occurred about 20 times a day lasting 30 seconds on average, pronounced autonomic phenomena accompanied the pain in terms of a strong reddening and lacrimation of the right eye and slight rhinorrhea. The conjunctival injection persisted after the headache and was observed also outside the SUNCT attacks.
Slow releasing carbamazepine was increased to 1,000 mg per day and methylprednisolone 16 mg was added. The combination of both drugs slightly reduced the frequency and the pain intensity of the SUNCT attacks. Soon after initiation of the combined therapy side effects including trepidation, tiredness, and vertigo appeared. Unfortunately, the patient suffered from a deep venous thrombosis of the right leg. Consequently the therapy with methylprednisolone was finished as quickly as possible. Alternatively, a medication with gabapentin was gradually increased to 3,600 mg and carbamazepine reduced to 400 mg, contemporaneously. Due to a persisting tremor carbamazepine was replaced by oxcarbazepine in the ratio 1:1.5 (600 mg). After the change to oxcarbazepine an obvious relief of the SUNCT attacks was accomplished. During the following 6 months gabapentin was gradually reduced to 400 mg. Under the therapy with oxcarbazepine (600 mg) and gabapentin (400 mg) the patient has a nearly complete relief of the symptoms for 36 months. Only slight periorbital dysesthesias and reddening of the right eye without the short lasting stabbing headache attacks were reported.

The patient’s history was unremarkable concerning relevant concomitant diseases. One and a half years and about 20 years ago a trigeminal neuralgia was reported, but the pain had disappeared spontaneously. His brother suffered from a trigeminal neuralgia and was treated by a microvascular decompression. A computed tomography scan of the brain revealed a small (0.5 x 1.0 cm) calcification in the right thalamus, microangiopathic changes, and enlargement of the internal ventricles. A magnetic resonance imaging scan of the brain, including the CISS-3D sequence of the cavernous sinus, showed no additional abnormalities. The neurological and ophthalmological examination (including the intraocular pressure), the cerebral spinal fluid pressure and analysis, and the serological examinations were in normal range.

**Comments**

We describe a 65-year-old man with a SUNCT syndrome that was responsive to the combination of oxcarbazepine and gabapentin. The reduction of either oxcarbazepine lower than 600 mg or gabapentin lower than 400 mg daily resulted in an exacerbation of the attacks, suggesting that the improvement of the cephalalgia was not due to spontaneous remission.

SUNCT syndrome belongs together with cluster headache and hemicrania continua to the group of trigeminal autonomic cephalalgias and was described as more or less untreatable for a long time [9]. To date, anticonvulsants seem to be the drugs of choice with preference for lamotrigine [7,10–12], topiramate [7,13–16], and gabapentin [7,17–19] (for review about all described cases see [7,8]). Partial improvement with carbamazepine was described in several patients [4,7,20]. The largest published cohort of patients with SUNCT syndrome reported 43 patients with therapeutic success rates of 68% for lamotrigine (to 400 mg daily), of 52% for topiramate (to 400 mg daily), of 45% for gabapentin (to 3,600 mg daily), and 39% for carbamazepine (to 900 mg daily) [7]. Only one report could be found in the literature that reported a dramatic response of SUNCT syndrome to oxcarbazepine (300 mg twice daily) [21]. Reports of the newer antiepileptic drugs pregabalin or levetiracetam or the intra-venous application of valproate acid are not available and might be used in therapy refractory SUNCT syndrome. Other therapeutic agents that have been tried in SUNCT, mostly with a disappointing effect, include NSAIDs, prednisone, ergotamine, dihydroergotamine, methysergide, sumatriptan, verapamil, valproate, lithium, propranolol, amitriptyline, and azathioprine [21]. In summary, all case reports that up to now have described a positive long-lasting therapeutic effect are dealing with drugs that act mainly in the central nervous system. This positive response is not surprising because SUNCT syndrome is generated and maintained in the central nervous system [22], and can be modulated or suppressed by stimulation of the posterior inferior hypothalamus [23].

Of special interest in this case is that the SUNCT syndrome responded to quickly titrated combination therapy. Advantages of this combination therapy are a faster control of symptoms in comparison with a slow titration of lamotrigine to avoid allergic reactions, and possibly reduced side effects due to only moderate dosages of both anticonvulsants. Performing a literature search in Medline we found only three case reports describing a combination therapy: one Indian patient received 600 mg carbamazepine and 100 mg lamotrigine daily and showed recurrence of symptoms being on either monotherapy; but after a few weeks lamotrigine has to be stopped due to leucopenia and resulted in a partial recurrence of pain [24]. The second patient showed partial relief of
symptoms under a combination therapy with 150 mg indomethacin and additional carbamazepine 800 mg daily [25]. The third patient received a dual therapy with carbamazepine and a short-time treatment with prednisolone for 16 days resulting in a complete relief and she did not complain about a recurrence of the pain being on monotherapy of carbamazepine [26].

Interestingly, our patient’s complains were first diagnosed as trigeminal neuralgia. During two weeks the character of the headache changed into the typical feature of the SUNCT syndrome with tearing and conjunctival injection. During the same time interval the initial good response to carbamazepine disappeared and the patient was admitted because of the pain exacerbation.

The likelihood that SUNCT and trigeminal neuralgia are intimately related has been discussed extensively [27,28], and coexistence of paroxysmal hemicrania, SUNCT syndrome, and trigeminal neuralgia is reported in two Italian patients [29]. From a pathophysiological point of view the trigemino-hypothalamic tract, a direct connection between the trigeminal nucleus caudalis and the posterior hypothalamus, has been described in rats and might be also responsible for an interaction of both structures in humans leading to a coincidence of trigeminal neuralgia and SUNCT syndrome or a conversion from trigeminal neuralgia into SUNCT syndrome [29]. Several cases have been reported with an initially classical neuralgic-type pain mutated over the years into typical SUNCT syndrome [30]. In these cases the pain became increasingly resistant to carbamazepine and the autonomic signs were more pronounced. In our case, the initial condition was highly suggestive of trigeminal neuralgia and SUNCT syndrome or a conversion from trigeminal neuralgia into SUNCT syndrome [29]. In these patients the pain became increasingly resistant to carbamazepine and the autonomic signs were more pronounced. In our case, the initial condition was highly suggestive of trigeminal neuralgia, but it was evident that despite slight changes in the clinical picture the most remarkable feature was the onset of the vasomotor phenomenon associated with the increased severity of pain as seen by the higher frequency and longer duration of the attacks and the absent refractory period.

Additionally, between the SUNCT attacks in our patient a periorbital edema and conjunctival injection were prominent that were probably due to a vasodilatation triggered by a parasympathetic activation even outside the attacks, as it has been reported for other SUNCT patients and cluster patients. A ptosis of the affected eye as in our patient has been described in only one SUNCT patient until now. This phenomenon may be explained as an incomplete Horner’s syndrome due to compression of sympathetic fibers caused by parasympathetic vasodilatation and vessel wall edema of the internal carotid artery [30].

In conclusion, the presented case suggests an alternative therapeutic regime with the combination of oxcarbazepine and gabapentin for SUNCT syndrome. Taken into account a fast up titration of both drugs and little side effects of the combined therapy, this therapeutic regime might be an alternative in comparison with the therapy with topiramate or lamotrigine, drugs that have to be increased over weeks to reach the therapeutic level.

References
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