Introduction

SUNCT syndrome (short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing) was first described in 1989 [1]. It is a rare and painful syndrome characterized by strictly unilateral, short-lasting (5–120 seconds) attacks associated with signs of local involvement of the autonomic system. The most important (so to be part of the acronym SUNCT) are conjunctival injection and tearing [2, 3]. Other signs are often, but not always, described: nasal stiffness, rhinorrhea, narrowing of the palpebral fissure, eyelid edema and miosis. These signs and symptoms are strictly ipsilateral to the pain. The pathophysiology of this headache form is still unknown. Goadsby and Lipton [4] proposed classifying SUNCT syndrome as a trigeminal autonomic cephalalgia (TAC), together with cluster headache (CH), chronic paroxysmal migraine (CPH), trigeminal neuralgia (TN) and others.

Case report

A 74-year-old man reported experiencing, since the age of 70 years, pain attacks involving first the forehead and the periorbital region, and then spreading to the nose and upper lip. These areas were involved strictly in the left side. The attacks had a high intensity and an abrupt onset, lasted 10–30 seconds and occurred almost every day between 6:00 and 8:00 AM or, more rarely, between 2:00 and 4:00 PM.

The treatment of SUNCT syndrome has been disappointing until 1999, when D’Andrea et al. [5] reported a therapeutic effect of lamotrigine. Based on the present case report of an elderly man with SUNCT, sodium valproate may also be an effective treatment for this debilitating headache.

Abstract

SUNCT syndrome (short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing) is a rare, debilitating headache that is difficult to be treated. We describe a SUNCT patient, initially treated with lamotrigine, with a positive response but with an unbearable side-effect (somnolence) that lead to withdrawal. The drug was replaced with sodium valproate at a dosage of 1000 mg b.i.d.. Complete remission of the attacks has been obtained for 1 year, without significant side effects.

Key words

SUNCT • Valproate • Treatment
Only occasionally (4–5 times during the previous 4 years) was a pain-free period of 1–3 months reported. The pain was described as burning or stabbing. Most of the attacks were triggered by shaving, slight touching of the skin of the involved region, washing the face or swallowing. No nausea, vomiting, photophobia or phonophobia was reported. The pain was regularly accompanied by signs of autonomic impairment: the most evident and invariably reported by the patient were tearing and conjunctival injection, but rhinorrhea and slight narrowing of the palpebral fissure were sometimes present. No changes in pupil diameter or in sweating pattern were observed. Each of these signs was strictly ipsilateral to pain, appeared at the onset of the attack and disappeared immediately or a few seconds after the end of pain.

Before his first consultation in our headache center, a diagnosis of cluster headache or trigeminal neuralgia had been supposed elsewhere and therefore he was being treated with several drugs (verapamil, carbamazepine, gabapentin, mexyletine, amitriptyline), without any improvement. A percutaneous retrogasserian glycerol rhizotomy had also been performed. Magnetic resonance imaging (MRI) had been performed twice during the 4 previous years and revealed, on both occasions, supratentorial hyperintensities on T2-weighted sequences (ischemic lesions). No lesions were detected in the brainstem or in the posterior fossa.

When the patient came to our attention, a diagnosis of SUNCT was made and therefore a treatment with lamotrigine, the first effective drug ever described, was started, at doses up to 100 mg/day. Complete remission was obtained, but the treatment had to be given up because of side effects (excessive somnolence). A few days after the discontinuation, the attacks reappeared. Then, a new prophylactic therapy with sodium valproate at increasing dosage up to 1000 mg b.i.d. was initiated. Within 20 days, the attacks completely ceased. It is interesting to note that when, 4 months after the beginning of therapy, he stopped taking valproate because of an ophthalmic intervention, the attacks immediately reappeared, but disappeared again 10–15 days after resuming valproate.

Since then (nearly 1 year ago) the patient is completely pain-free. The therapy is well tolerated. Serum drug concentration ranges from 55 to 60 µg/ml (therapeutic range, 40–100).

Discussion

The present case fulfils the diagnostic criteria for SUNCT proposed by Goadsby and Lipton [4], with the particular aspect of the location of pain, which in our patient is larger, involving not only the orbital region, but also spreading to the nose and upper lip. The area corresponding to the first branch of the trigeminal nerve is the most commonly reported, but other parts have been described as well [2, 6–8].

Sodium valproate is an antiepileptic drug in use since the end of the 1960s. The anticonvulsant action is due to the inhibition of voltage-dependent Na+ channels and a GABAergic mechanism (stimulation of brain GABA synthesis, inhibition of GABA reuptake and GABA amino-transferase, activation of glutamic acid decarboxylase). On the other hand, sodium valproate reduces glutamate levels, one of the excitatory neurotransmitters, by increasing the activity of glutamic acid decarboxylase. The enhancement of GABA activity is thought to be the mechanism in preventing migraine attack [5]. Several clinical studies have demonstrated the efficacy of sodium valproate as prophylactic agent in migraine [9, 10]. The drug was therefore recently included in the Italian [11] and American guidelines [12] on diagnosis and treatment of migraine, at dosages of 800–1500 mg/day.

No effective treatment for SUNCT was known until 1999, when D’Andrea et al. [5] reported a positive response to lamotrigine. This is a new antiepileptic drug, whose main mechanism of action is the inhibition of release of glutamate, through the blockade of voltage-dependent Na+ channels. Since then other cases have been reported to be responsive to the drug [13, 14]. A positive response to gabapentin, another new antiepileptic drug with a GABAergic action, has been observed as well [6].

Before the patient’s first consultation in our headache center, he had been treated with several drugs commonly used in TN (e.g. carbamazepine, gabapentin, mexyletine, amitriptyline) and in CH (verapamil), without any appreciable result. Apart from lamotrigine, only few drugs have some beneficial effect in treating SUNCT: carbamazepine is the most frequently reported (having a possible partial positive effect), but also prednisone, nifedipine, sumatriptan and azathioprine have been claimed to be effective in single patients [2, 15]. The lack of definite effect of most drugs commonly used against TN and CH (verapamil even seems to worsen pain) [4, 15] suggests that SUNCT has a distinct nosologic position among TACs, though it shares common pathophysiologic aspects [7]. Moreover, the therapeutic response [7, 16], together with clinical criteria [17], plays a role in the differential diagnosis among TN and other short-lasting headaches.

Although we obtained a good clinical response with lamotrigine in our patient with SUNCT, we had to interrupt the treatment because of side effects (excessive sedation).

This is not the first time in which sodium valproate is used in prevention of SUNCT syndrome. In 1995, Pareja et al. [15] reported 3 cases treated with valproate, but in only one of them a “possible slight improvement” was described. So, our case could be the first with a definite positive result.
cannot definitely exclude that the therapeutic response is due to a placebo effect. Nevertheless, it is noteworthy that we observed a temporary worsening of the attacks, exactly during the period of withdrawal.

We cannot explain why valproate is effective in preventing SUNCT. Probably, either an antiglutamatergic or a GABAergic mechanism is involved. In the first case, the action is similar to that of lamotrigine; in the second case, the mechanism resembles that of gabapentin. Both mechanisms support the hypothesis of a neurally mediated nociceptive component. Further confirmations of the effectiveness of sodium valproate in SUNCT syndrome are required, and more details about the pathophysiology of SUNCT are needed, in order to define the role of this drug in treating SUNCT. If our result will be confirmed, sodium valproate could become an interesting second-choice drug in the treatment of SUNCT.

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