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Case Report

Short-lasting unilateral neuralgiform headache with conjunctival injection and tearing: Response to antiepileptic dual therapy

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Short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT) is included among trigeminal autonomic cephalalgias in the International Classification of Headache Disorders-2. Available literature suggests that it responds to anticonvulsants, particularly lamotrigine. However, management of partial responders is difficult and antiepileptic duo-therapy may be an answer to it. Nonetheless, to our knowledge, anticonvulsant combination has never been tried in partial responders to monotherapy.

We are presenting a case of SUNCT that had overlapping symptoms with Short-lasting Unilateral Neuralgiform headache attacks with cranial Autonomic features and responded well only to the combination of lamotrigine with carbamazepine. However, lamotrigine had to be stopped as patient developed leucopenia and it resulted in partial recurrence of symptoms.

**Key words:** Anticonvulsants, lamotrigine, leucopenia, short-lasting unilateral neuralgiform headache attacks with cranial autonomic features, short-lasting unilateral neuralgiform headache with conjunctival injection and tearing

Short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT) is characterized by short-lived, strictly unilateral, moderate to severe pain attacks in the orbital area and is accompanied by conjunctival injection and lacrimation. It can be primary or secondary; the latter being commonly associated with lesions of the posterior fossa or pituitary adenoma. It is refractory to many of the commonly employed therapies but the patient may benefit from a variety of antiepileptics e.g. carbamazepine, topiramate, lamotrigine, gabapentin and oxcarbazepine. Among these lamotrigine is the most effective treatment. Though reviews based on open-labeled trials are available to the best of our knowledge, randomized controlled trials are not available. In addition, most of the anecdotes describe those subjects who responded to a single antiepileptic but use of antiepileptic duo-therapy in SUNCT has probably never been reported. Both lamotrigine and carbamazepine are known to cause leucopenia, albeit rarely.

We are presenting a case of SUNCT that responded partially to monotherapy of either carbamazepine or lamotrigine but attained complete remission when the combination of these drugs was prescribed. However, despite remarkable improvement of symptoms, combination therapy had to be stopped as the patient developed leucopenia, which improved on stopping lamotrigine.

**Case Report**

A 45-year-old man presented with complaints of multiple episodes of strictly right-sided supraorbital-temporal burning pain; each episode lasting from a few seconds to a few minutes. The pain was localized and non-radiating and recurred at the same site each time. It used to start or aggravate by air-breeze or blow of air, touching the eyebrow or combing his hair. It was associated with ipsilateral lacrimation, conjunctival injection and rhinorrhea that lasted for the period of pain.

His past history was unremarkable and family history did not contribute anything to the diagnosis. He was diagnosed as Trigeminal Neuralgia in the past and was prescribed carbamazepine 600 mg/day that offered only partial relief. General physical examination and neurological examination as well as the neuroimaging did not reveal any abnormality.

Diagnosis of SUNCT was made and baseline investigations (complete blood counts and liver function tests) were ordered. Since lamotrigine had shown promising results in the management of SUNCT, he was gradually shifted from carbamazepine 600 mg/day to lamotrigine 100 mg/day over four weeks. Further
treatment was governed by symptom severity and blood counts. The patient responded well to a combination of lamotrigine and carbamazepine while the antiepileptic monotherapy was associated with symptom recurrence. He developed leucopenia i.e. total leucocyte count less than 4500/cumm\(^9\) after 2.5 months of lamotrigine and carbamazepine dual therapy, which improved with the reduction of lamotrigine; re-challenge worsened it and withdrawal of lamotrigine again improved leucopenia but with the recurrence of symptoms. Due to ethical considerations patient could not be switched to lamotrigine monotherapy again.

**Discussion**

Firstly, diagnostic confusion was apparent in this patient as he was diagnosed as a case of trigeminal neuralgia in the past. Mechanical trigger factors were reported by the patient and, they have also been described in SUNA (Short-lasting Unilateral Neuralgiform headache attacks with cranial Autonomic features) and SUNCT.\(^{[2,3,10]}\) Unlike trigeminal neuralgia, in the present case the pain was present in the area of the first division of the trigeminal nerve and was accompanied by cranial autonomic symptoms.\(^{[1,10]}\) Shorter duration of attacks differentiated it from cluster headache and paroxysmal hemicrania.\(^{[6]}\) Exact taxonomic placement of this patient is difficult even with the ICHD-2 classification owing to overlapping features of SUNCT and SUNA. According to ICHD-2, besides temporal or orbital stabbing pain, SUNCT attacks are characterized by conjunctival injection and tearing both, occur at a higher frequency of three to 200 times a day\(^{[1,10]}\) and each attack lasts for 5-240 s. The SUNA attacks are similar to SUNCT in anatomical distribution and quality of pain but their individual episodes may last longer (2 s to 10 min), are less frequent and are accompanied by any one of the cranial autonomic symptoms including rhinorrhea. Cohen et al.\(^{[10]}\) recently reviewed cases of SUNCT and SUNA and according to their proposed guidelines, SUNA attacks cannot have conjunctival injection and tearing together, while they reported other cranial autonomic symptoms e.g. nasal blockade, rhinorrhea, eyelid edema, ptosis etc. in approximately half of their SUNCT patients. Based on these evidences, diagnosis of SUNCT was made, instead of SUNA.

Secondly, as we have already mentioned, randomized controlled trials for the management of short lasting unilateral neuralgiform headache attacks are not available and the literature advocates the efficacy of anticonvulsants in SUNCT. Contrary to the present report, most of the case reports in the past had described complete remission of SUNCT with lamotrigine monotherapy.\(^{[2-4]}\) To achieve better control of symptoms in the present patient we decided to combine two anticonvulsants which is a common method for refractory cases of epilepsy and mania. It should be noted here that the combination of drugs is described to be more efficacious in controlling symptoms along with the minimization of dose-dependent adverse effects.\(^{[11]}\) Probably, both the drugs acted synergistically to suppress all the symptoms in this case. It should be recognized that insufficient duration and suboptimal doses of lamotrigine could be one reason behind the poor response to lamotrigine monotherapy in this case. At least one previous report suggests complete remission with 300 mg/day lamotrigine and that too, after approximately two months of continuous treatment.\(^{[4]}\) Unfortunately, because of the symptom recurrence and risk of potential adverse effects with higher dose we could not keep the patient on lamotrigine monotherapy or escalate its dose.

Thirdly, it is difficult to find out what caused leucopenia in this case. Carbamazepine was well tolerated for a long period, as was the lamotrigine monotherapy for at least two months. Leucopenia developed when the patient was switched to dual therapy of carbamazepine and lamotrigine to achieve better control of symptoms. It suggests that the combination rather than lamotrigine alone could be the causative factor. Moreover, lamotrigine-induced hematological abnormalities may appear after eight weeks of therapy and are reversible with the discontinuation of the drug.\(^{[12,13]}\) At this stage we do not have sufficient evidence to rule out any of the possibilities. Our hypothesis (that lamotrigine-induced leucopenia) is substantiated by the fact that leucocyte count increased after withdrawing it and again decreased with the re-challenge. It suggests that lamotrigine as monotherapy and the combination of lamotrigine with carbamazepine as well should be used cautiously with regular hematological monitoring.

In summary, besides emphasizing further research regarding clinical features of SUNCT and SUNA, the present case highlights the fact that dual antiepileptic therapy may be beneficial to subjects whose headache is refractory to anticonvulsant monotherapy. However, considering the possibility of potential adverse effects, such patients should be closely monitored during the course of treatment.

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