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Letter to the Editor

Scalp allodynia-precipitating seizures in a girl after starting topiramate

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We are reporting the case of a 9-year-old girl with left sided complex partial epilepsy who developed scalp allodynia after commencing topiramate. She first had seizures at the age of 6 weeks. Apart from having epilepsy, she is generally healthy and making normal educational progress. Her electroencephalographs have shown some bursts of irregular spike wave activity particularly in the right central region. A computerize tomography brain scan and two magnetic resonance imaging brain scans, one performed recently, have been normal. Initially her epilepsy responded to phenobarbitole and she remained seizure free for 3 years after it was stopped. At the age of 5 years, she had a recurrence of seizures. During these episodes, she turned her head to the left and had left leg jerking associated with confusion and at times loss of consciousness. Her seizures were occurring several times a week. Subsequently, she was prescribed various antiepileptic drugs (AEDs) including carbamazepine, sodium valproate and levetiracetam as monotherapies and in combination. Most of the AEDs initially did have a beneficial effect but seizure control wore of quickly. After starting topiramate, levetiracetam dose was gradually reduced and subsequently stopped. The starting dose of topiramate was 0.5 mg/kg at night and was gradually increased to 9.0 mg/kg/day in two divided doses. Her seizure control initially improved on topiramate monotherapy but at the dose of 9.0 mg/kg/day, she developed a painful and sensitive scalp (allodynia) especially on the left side. The extent of severity of this allodynia was such that combing her hair or even touching her scalp on the left side would trigger a seizure, the semiology of which was similar to her previous seizures. Due to her severe allodynia it was impossible to attach the electrodes to perform a repeat electroencephalograph. After stopping topiramate the symptoms of the scalp allodynia resolved completely. Currently her seizures are controlled on clobazam and gabapentine. Our search of existing literature has shown that hyperesthesia or allodynia caused by topiramate have not been reported previously.

Allodynia is defined as a pain resulting from an innocuous non-painful stimulus to normal skin or scalp. The pain can be provoked by combing hair, shaving, showering and even wearing glasses. It is more commonly seen in females and often associated with a high headache frequency, increased body mass index, disability and depression [1]. Allodynia is a clinical feature of many painful conditions such as neuropathies, post herpetic-neuralgia, fibromyalgia, and migraine. It is more common and severe in migraines than in pri-

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mary headaches [1]. The allodynia and hyperalgesia observed in some cases after the administration of morphine are due to interference with normal inhibitory processes [2]. The cell types involved in nociception and mechanical sensation are the cells responsible for allodynia [3].

Interestingly topiramate is effectively used in the treatment of various pain syndromes in which allodynia is often a recognized component, such as cluster headache, migraine, reflex sympathetic dystrophy, idiopathic facial pain, diabetic peripheral neuropathy and others. Topiramate is one of the widely used newer AEDs as a monotherapy or in combination with other AEDs for both focal and generalized epilepsies. It is typically added to the treatment regimen when other AEDs fail to control seizures [4]. Topiramate has minimal hepatic drug interactions, it does not require serum drug concentration monitoring, it has a high therapeutic index and it is well tolerated and can be used at doses greater than the recommended maximum dose [5–7]. The most common side effects are central nervous system related and include dizziness, fatigue, visual disturbances, ataxia, mental slowing and impaired concentration. Paresthesias, anorexia, weight loss, anhydrosis, hypohydrosis, hyperthermia and increased risk of nephrolithiasis have been also reported [8–10]. Most of the side effects from topiramate are dose dependant but tolerance can be achieved by starting with a lower dose and slowly titrating upwards [11–13]. It has been postulated that the antiepileptic and analgesic effects of topiramate are due to its action on neuronal transmission in at least five ways including modulating sodium ion channels, potentiating GABA inhibition, blocking excitatory glutamate neurotransmission, modulating calcium ion channels and by inhibiting carbonic anhydrase [13]. In our case, we therefore report a paradoxical effect of topiramate of inducing allodynia that in turn precipitated seizures.

We report allodynia after starting topiramate, resolving completely after withdrawing. We hypothesise that this side effect may be due to topiramate inducing peripheral nerve hyperactivity. This may have occurred via the inhibition of carbonic anhydrase isoenzyme which may lead to hyperactivity of periphral nerves then allodynia [14,15]. Nevertheless, allodynia may also have been triggered by a sterile inflammatory response caused by topiramate cortical depression leading to substance P and calcitonin gene-related peptide release followed by activation of trigeminal neurons [16].

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