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Refractory short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing responsive to anti-calcitonin gene-related peptide monoclonal antibodies: A case report

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Abstract

Background: Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) is a rare but severely disabling variant within the spectrum of trigeminal autonomic cephalalgia lacking evidence-based treatment.

Case: We report a case of chronic SUNCT in a 67-year-old man refractory to various guideline-conforming treatment attempts responding excellently to galcanezumab.

Conclusions: This case report indicates that monoclonal antibodies against calcitonin gene-related peptide, specifically galcanezumab, might be a treatment option for SUNCT warranting further investigation.

Keywords

SUNCT, CGRP, treatment

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Case report

A 67-year-old man was admitted to our neurology service with a 10-year history of strictly left-sided, frontoorbital headache attacks lasting 60–120 sec occurring approximately 50 times a day. The pain character was described as "burning needles" with an intensity of 7–9 on the visual analogue scale (VAS). These attacks were always accompanied by ipsilateral ptosis, tearing, conjunctival injection and rhinorrhea. Attacks occurred chronically during the whole year without extended attack-free intervals, with frequent accumulation in the months from February to May. Attacks strongly impacted the patients' quality of life as he could not participate in social activities and became increasingly withdrawn from social life. The patient did not report other headache symptoms or any relevant medical history. He had a family history of migraine on the mother's side but did not report migrainous symptoms himself.

Extensive diagnostic work-up including neurological examination, brain MRI (T1, gadolinium enhanced T1, T2 and diffusion-weighted sequences including a trigeminal protocol for detection of vascular nerve contact), CT scan for bone alterations and laboratory investigations were unremarkable.

Consequently, after exclusion of secondary causes, the diagnosis of chronic short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) was established according to current criteria (1).

At the time of admission, the patient had already undergone unsuccessful treatment trials with

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indomethacin (150 mg/day), carbamazepine (maximum dosage 600 mg/day), lamotrigine, gabapentin (maximum dosage 1800 mg/day), verapamil, zolmitriptan and opiod-analgetic blockade of the ganglion cervicale superius, which were all discontinued due to inefficacy.

In June 2019, topiramate (titrated up to 200 mg per day) was initiated without change of attack frequency (~ 50/day), VAS (7–9) or attack duration (60–120sec) after 4 months of administration.

After exclusion of potential contraindications such as cardiovascular diseases and diligent and extensive information for the patient, including written informed consent, we initiated the anti-calcitonin gene-related peptide (CGRP) monoclonal antibody (MAB) erenumab 140 mg as an off-label individual treatment approach. The patient did not report any adverse events during treatment with erenumab. After 3 days, the patient reported complete remission of attacks, but attacks resurfaced 3 weeks after erenumab application. We readministered erenumab 140 mg 4 weeks after initial application: Again, the patient reported complete remission of attacks with recurrence of attacks after 3 weeks. Thus, we assumed a wearing-off effect and opted for changing to galcanezumab (initial loading dose 240 mg) 5 weeks after the second application of erenumab. The patient reported complete remission of attacks within 2 days. Galcanezumab was continued at 120 mg every 4 weeks, with complete remission holding up now for 6 months and ongoing without experiencing any side effects or adverse events (Figure 1).

The patient gave written consent to anonymised publication of his case.

Discussion

To date, there is no evidence-based treatment for SUNCT/SUNA. Owing to its rarity, randomised controlled trials are hardly feasible and treatment algorithms are based on case series and expert opinions. Treatment partly effective in other trigeminal autonomic cephalalgias (TACs), such as indomethacin, high-flow oxygen inhalation, sumatriptan and verapamil, are ineffective in SUNCT/SUNA (2). For short-term prevention, intravenous lidocaine by infusion has shown some efficacy, but necessitates observation and is often not well tolerated. For long-term prevention, topiramate and lamotrigine are efficacious in preventing SUNCT/SUNA attacks (3). However, there is a relevant proportion of patients who are refractory or intolerant to the current standard medical treatment.

In addition to pharmacological treatment, there are some experimental approaches comprising peripheral neuromodulation (greater occipital nerve region injections with corticosteroids and local anesthetics, occipital nerve stimulation) or even central neuromodulation (deep brain stimulation in the ipsilateral posterior hypothalamus, high cervical spinal cord stimulation). While there have been some case reports of successful application of these approaches, they are mostly invasive and carry significant risks (4).

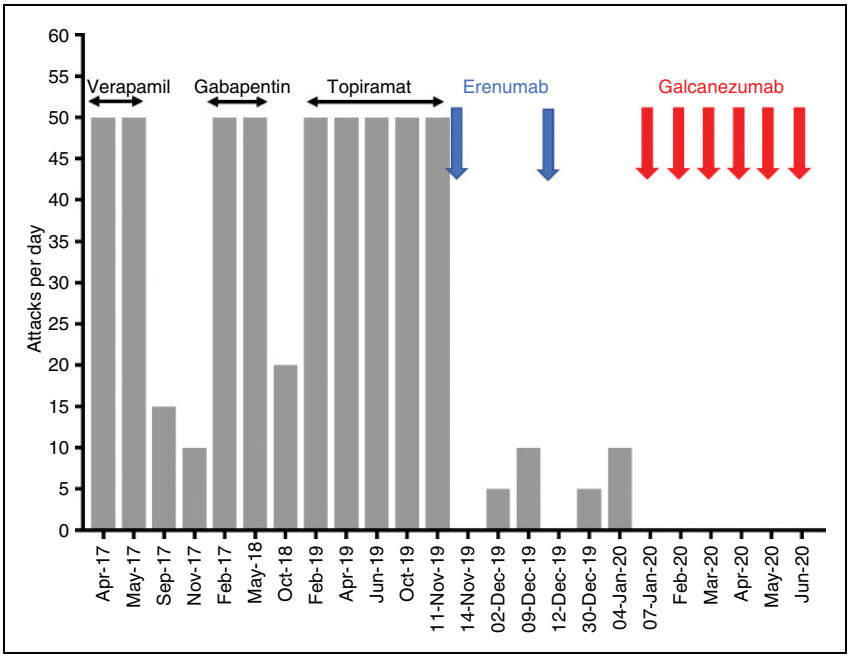

Figure 1. Course of mean daily number of attacks and preventive therapies. Number of attacks determined by headache diary. Data is shown in monthly intervals except for erenumab, which is shown in weekly intervals to highlight details.

Our patient is a textbook case of treatment-refractory chronic SUNCT significantly impacting quality of life.

The implementation of CGRP pathway blockade with MAB has revolutionised treatment and prevention of migraine, with unprecedented responder rates and tolerability similar to placebo (5). Recently, galcanezumab has also proven effective and subsequently was licensed by the FDA for preventing episodic cluster headache, the most frequent disease within the TAC spectrum (6,7). Considering the supposedly similar underlying biology, anti-CGRP-MABs, specifically galcanezumab, might also be effective in other TACs such as SUNCT/SUNA (8). However, to date anti-CGRP-MABs have not yet been tried in SUNCT/SUNA and there are no case reports either. It was recently speculated that there may be an underlying or background migrainous biology in SUNCT/SUNA (defined as presence of nausea, photo- or phonophobia, or a family history of migraine) providing an additional rationale for anti-CGRP-MABs in SUNCT/SUNA (9).

Since our patient displayed severe, treatment-refractory SUNCT with signs of an underlying migrainous biology, we thus opted for using off-label erenumab and galcanezumab, resulting in excellent response over more than 6 months. Blockade of the CGRP pathway was effective in our patient both by inhibition of the CGRP receptor (erenumab) and CGRP ligand (galcanezumab), thus arguing for an important role of CGRP in the pathophysiology of SUNCT. Efficacy of erenumab seemed to show a wearing-off effect, which has also been reported in a proportion of migraine patients treated with erenumab but not galcanezumab (10,11). After switching to galcanezumab, we did not observe a further wearing-off effect. This might indicate that ligand blockade could be more effective than receptor blockade in SUNCT.

Of note, looking at the general course of attack frequency, we noticed a seasonal pattern with declining attack frequency in autumn. Indeed, verapamil and gabapentin were each discontinued before attack frequency started to decline, thus the decrease in attack frequency occurred either seasonally or coincidentally. While SUNCT/SUNA is usually described as having an irregular temporal pattern with symptomatic periods alternating with remissions in an erratic fashion, there are some reports of patients displaying a seasonal pattern (12,13). Although the underlying pathophysiology is unclear, a hypothalamic involvement has been suggested similar to other TACs, which likely share some pathophysiological mechanisms (14).

In conclusion, we report a case of previously treatment refractory chronic SUNCT responding excellently to galcanezumab. This case report indicates that galcanezumab might be a treatment option for SUNCT warranting further investigation.

Clinical implications

- We report a case of chronic SUNCT in a 67-year-old man refractory to various guideline-conforming treatment attempts responding excellently to galcanezumab.
- This case report indicates that monoclonal antibodies against calcitonin gene-related peptide, specifically galcanezumab, might be a treatment option for SUNCT warranting further investigation.

Author contributions

GB: Patient recruitment, acquisition of data, drafting manuscript; CB: Patient recruitment, acquisition of data, critical revision of manuscript for intellectual content; GBr: Critical revision of manuscript for intellectual content.

Declaration of conflicting interests

The authors declared the following potential conflicts of interest with respect to the research, authorship, and/or publication of this article: GB has participated in meetings sponsored by, received speaker honoraria or travel funding from Biogen, Celgene, Merck, Novartis, Sanofi-Genzyme, Roche and Teva, and received honoraria for consulting from Biogen, Roche and Teva.

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