Research Square

Preprints are preliminary reports that have not undergone peer review.
They should not be considered conclusive, used to inform clinical practice,
or referenced by the media as validated information.

Preventive CGRP ligand monoclonal antibody therapy in refractory adult-onset migraine-associated cyclic vomiting syndrome

Gonçalo Cabral

goncalo2010286@gmail.com

Hospital de Egas Moniz, Unidade Local de Saúde de Lisboa Ocidental

Alexandra Martins

Hospital de Egas Moniz, Unidade Local de Saúde de Lisboa Ocidental

Miguel Viana Baptista

Hospital de Egas Moniz, Unidade Local de Saúde de Lisboa Ocidental

---

Case Report

Keywords: Cyclic Vomiting Syndrome, CGRP-Targeted Therapy, Migraine

Posted Date: March 25th, 2026

DOI: https://doi.org/10.21203/rs.3.rs-8981588/v1

License: This work is licensed under a Creative Commons Attribution 4.0 International License.
Read Full License

Additional Declarations: No competing interests reported.

Abstract

Cyclic vomiting syndrome (CVS) is a disorder of gut–brain interaction frequently associated with migraine, suggesting overlapping neurobiological mechanisms. However, therapeutic options remain limited in refractory adult patients. Calcitonin gene-related peptide (CGRP) plays a central role in migraine pathophysiology and is also involved in visceral sensory processing, nausea, and autonomic regulation, supporting a potential therapeutic role for CGRP-targeted therapies in selected CVS phenotypes. We report a 51-year-old woman with adult-onset migraine-associated CVS refractory to multiple preventive therapies, including amitriptyline, venlafaxine, and topiramate. Preventive treatment with the CGRP ligand monoclonal antibody fremanezumab resulted in a marked reduction in migraine frequency and substantial improvement in vomiting severity and frequency, with significant functional recovery over six months of follow-up. This observation supports the hypothesis that CGRP modulation may benefit selected patients with migraine-associated CVS and highlights the need for further systematic evaluation of CGRP-targeted therapies in disorders of gut–brain interaction.

Introduction

Cyclic vomiting syndrome (CVS) is a disorder of gut–brain interaction characterized by recurrent and stereotyped episodes of severe nausea and vomiting and is increasingly recognized in adults.[1,2] CVS is frequently associated with migraine, suggesting shared neurobiological mechanisms, although therapeutic options remain limited in refractory patients. Calcitonin gene-related peptide (CGRP) plays a central role in migraine pathophysiology and is also involved in nausea, visceral afferent signalling and autonomic regulation.[1–3] However, clinical evidence supporting CGRP-targeted therapies in CVS remains scarce.

Case Description

A 51-year-old woman with hypertension, asthma, depression and anxiety disorder developed episodic migraine without aura and recurrent vomiting episodes concomitantly in early adulthood, fulfilling the International Classification of Headache Disorders, 3rd edition (ICHD-3) criteria for migraine.[4] She was evaluated in Internal Medicine and Gastroenterology clinics, and alternative metabolic, gastrointestinal, endocrine and structural causes of recurrent vomiting were systematically excluded. The clinical presentation fulfilled Rome IV diagnostic criteria for cyclic vomiting syndrome.[5] Attacks occurred approximately four days per month and typically lasted 24–48 h. Migraine attacks were associated with intense nausea and frequent, uncontrollable vomiting (> 4 emetic episodes per hour at peak intensity and > 10 vomiting episodes per day), leading to recurrent work absenteeism. Vomiting episodes were temporally related to migraine attacks. Intranasal zolmitriptan was the only consistently effective abortive therapy for headache. Acute emetic episodes were unresponsive to metoclopramide or domperidone. Preventive trials with amitriptyline (up to 50 mg/day), venlafaxine (up to 150 mg/day) and topiramate (up to 100 mg/day) were each administered for at least three months at therapeutic doses,

with only marginal benefit. Preventive therapy with fremanezumab 225 mg monthly was initiated primarily for migraine prevention. During six months of follow-up, migraine frequency decreased from approximately four days per month to one day per month, and the severity and frequency of nausea and vomiting were substantially reduced. Functional improvement was significant, with complete resolution of work absenteeism, during six months of follow-up. No blood pressure elevations or other adverse events were observed.

Discussion

This report describes a single clinical observation of improvement of refractory adult-onset migraine-associated CVS following preventive CGRP ligand monoclonal antibody therapy. While CGRP is well established in migraine biology and gastrointestinal sensory processing, its contribution to CVS remains incompletely understood and likely heterogeneous.[3] Similar benefit from CGRP-directed therapy has recently been reported in related gut–brain interaction disorders, such as abdominal migraine, supporting the biological plausibility of CGRP modulation in selected phenotypes.[6] However, available evidence remains limited, given the refractory nature of CVS in many adults and the limited effectiveness of existing treatments, carefully documented clinical observations remain important to identify potentially responsive patient subgroups and to support further systematic evaluation of preventive CGRP-directed therapies in migraine-associated CVS.

Declarations

Ethical approval:

Ethical approval was not required for this study, as it is a single case report with no experimental intervention. Written informed consent was obtained from the patient for publication of this case report and any accompanying data.

Conflict of Interest:

The authors declare that they have no conflicts of interest relevant to this work.

Consent to Publish

Written informed consent was obtained from the patient for publication of this case report and any accompanying data.

Funding:

This research did not receive any specific grant from funding agencies in the public, commercial, or not-for-profit sectors.

Author Contribution

1- All authors contributed equally to this work.

References

1. Venkatesan T, Levinthal DJ, Tarbell SE, et al. Guidelines on management of cyclic vomiting syndrome in adults by the American Neurogastroenterology and Motility Society and the Cyclic Vomiting Syndrome Association. Neurogastroenterol Motil. 2019;31(Suppl 2):e13604. 10.1111/nmo.13604.
2. Russell FA, King R, Smillie SJ, et al. Calcitonin gene-related peptide: physiology and pathophysiology. Physiol Rev. 2014;94:1099–142. 10.1152/physrev.00034.2013.
3. Kovacic K, Li BUK. Cyclic vomiting syndrome: A narrative review and guide to management. Headache. 2021;61:231–43. 10.1111/head.14073.
4. Headache Classification Committee of the International Headache Society. The International Classification of Headache Disorders, 3rd edition. Cephalalgia.. 2018; 38:1–211. 10.1177/0333102417738202
5. Drossman DA, Hasler WL. Rome IV—Functional gastrointestinal disorders: Disorders of gut–brain interaction. Gastroenterology. 2016;150:1257–61. 10.1053/j.gastro.2016.03.035.
6. Baskaran T, Beier D. Calcitonin gene-related peptide–targeting drugs efficiently treat abdominal migraine: a case report. Cephalalgia Rep. 2025. 10.1177/25158163251341303.