

# Cyclic Vomiting Syndrome: An underdiagnosed entity. Report of a case

Síndrome de Vómito Cíclico: Una entidad infradiagnosticada. Reporte de un caso

Florencia Rodríguez <sup>1</sup>, Ignacio Moratorio <sup>2</sup>, Virginia López <sup>3</sup>, Carolina Olano <sup>4</sup>

<sup>1</sup> Postgrado, Clínica de Gastroenterología Montevideo, Uruguay.

<sup>2</sup> Asistente, Clínica de Gastroenterología Montevideo, Uruguay.

<sup>3</sup> Profesora Agregada, Clínica de Gastroenterología Montevideo, Uruguay.

<sup>4</sup> Profesora, Clínica de Gastroenterología Montevideo, Uruguay.

Recibido: 07/08/22 - Aprobado: 11/12/22

## ABSTRACT

Cyclic vomiting syndrome is a benign, chronic, functional gastrointestinal pathology that manifests clinically with intense nausea and vomiting interspersed with asymptomatic periods. Its diagnosis is made according to the Rome IV criteria, which require the presence of at least 2 episodes of vomiting in the past 6 months or 3 or more episodes in the past year, with the corresponding exclusion of secondary causes that can explain the vomiting. We present the case of a 44-year-old man who consulted for intermittent nausea and vomiting of 1 year evolution with hydroelectrolytic repercussion and multiple emergency consultations. The diagnosis of cyclic vomiting syndrome was made and treatment with amitriptyline was started due to its neuromodulatory effect to prevent the recurrence of episodes. After 6 months of establishing it, the patient is asymptomatic.

**Keywords:** Vomiting; Amitriptyline (source: MeSH NLM).

## RESUMEN

El síndrome de vómitos cíclicos es una patología gastrointestinal funcional crónica, benigna, que se manifiesta clínicamente con náuseas y vómitos intensos que intercalan con periodos asintomáticos. Su diagnóstico se realiza de acuerdo con los criterios de Roma IV, que requieren la presencia de al menos 2 episodios de vómitos en los últimos 6 meses o 3 o más episodios en el último año, con la correspondiente exclusión de causas secundarias que puedan explicar los síntomas. Se presenta el caso de un hombre de 44 años que consulta por náuseas y vómitos intermitentes de 1 año de evolución, con repercusión hidroelectrolítica y múltiples consultas en emergencia. Se realiza el diagnóstico de síndrome de vómitos cíclicos y se inicia tratamiento con amitriptilina, por su efecto neuromodulador para prevenir la recurrencia de los episodios. Luego de 6 meses de instaurado el mismo, el paciente se presenta asintomático.

**Palabras clave:** Vómitos; Amitriptilina (fuente: DeCS Bireme).

## INTRODUCTION

CVS is a rare, chronic disorder characterized by acute, stereotyped episodes of severe nausea and vomiting, alternating with asymptomatic periods.<sup>1,2</sup>

The incidence of this pathology is unknown in adults, but it is estimated that between 3-14% of patients are referred for unexplained nausea and vomiting. Its prevalence is slightly higher in Caucasian and young men with a mean age of 25 years.<sup>3</sup> There is a delay in diagnosis, since vomiting can be attributed to other pathologies, and it is common for there to be multiple consultations prior to diagnosis.<sup>2,4,5</sup>

According to Rome IV criteria, CVS implies the presence of at least 2 episodes of vomiting lasting less than 7 days in the past 6 months or 3 or more episodes

in the past year. Systemic diseases that may explain the symptoms should be excluded.<sup>1,3</sup>

CVS typically comprises 4 phases: pre-emetic period with pallor, diaphoresis, and nausea, followed by hyperemesis with up to 30 episodes per day, often with associated epigastric or diffuse abdominal pain and/or diarrhea.<sup>3</sup> Subsequently, a recovery phase with gradual resolution of symptoms and finally remission or inter-episodic phase.<sup>1,2</sup>

Multiple theories have been proposed to understand the pathophysiological mechanism underlying CVS. The most accepted one establishes that the syndrome is triggered by psychological or infectious phenomena, which lead to alterations in the autonomic pathways of the brain-gut axis. The association with migraines supports an underlying stress-sensitive mechanism.<sup>2,4</sup>

Citar como: Rodríguez F, Moratorio I, López V, Olano C. Cyclic Vomiting Syndrome: An underdiagnosed entity. Report of a case. *Rev Gastroenterol Peru.* 2022;42(4):257-60. doi: 10.47892/rgp.2022.424.1404

Other triggers can be sleep deprivation, food such as chocolate, cheese and monosodium glutamate, motion sickness and drugs from the opiate group.<sup>1,6</sup>

Treatment of CVS lies in identifying and avoiding triggering factors, preventing recurrence, as well as complications during acute episodes.<sup>1,2</sup> During hyperemesis, adequate fluid and electrolyte replacement must be guaranteed, generally intravenously, as well as antiemetic drugs.<sup>7</sup> 5-HT<sub>3</sub> antagonists, such as Ondansetron, are superior to dopaminergic receptor antagonists such as Domperidone, in symptomatic control.<sup>1,7</sup>

For the prevention of recurrences, tricyclic antidepressants (TCAs) or anticonvulsants are used when they do not respond to TCAs.<sup>1,2</sup>

The following clinical case is described in order to make the medical team aware of this pathology, which requires high clinical suspicion for its diagnosis.

## CLINICAL CASE

The case of a 44-year-old male nurse from the department of Paysandú is presented. From his personal history, he was diagnosed with non-insulin-dependent diabetes mellitus in 2013, in treatment with Metformin 500 mg every 6 hours with good metabolic control, without target organ damage. Dyslipidemia in treatment with Rosuvastatin 40 mg; former smoker; presents anxiety disorder in treatment with Alprazolam 1 mg and intermittent throbbing hemicranial headaches without current treatment.

Nine months prior to consultation, the patient attended the emergency room due to biliary colic, nausea and vomiting after taking cholecystokinetics. Acute gallstone cholecystitis was diagnosed, and emergency cholecystectomy was performed. He did not present immediate postoperative complications. Fifteen days later, he returned with abundant, intermittent vomiting, requiring hospital admission for fluid and electrolyte replacement and antiemetic treatment, with partial improvement. Magnetic resonance cholangiopancreatography was requested, which did not show lesions nor the presence of residual stones, and the routines were normal.

The patient persisted with nausea and vomiting for several months and consulted in the Gastroenterology Service. Video gastroscopy was requested, which did not show any lesions. Abdominal computed tomography (CT) showed a 35-mm left adrenal adenoma. Hypercortisolism was ruled out as a secondary cause of vomiting, with a negative Nugent test. Head CT did not report any lesions.

Given the chronology of symptoms and the exclusion of other pathologies that could explain the symptoms, a diagnosis of CVS was made. Symptomatic treatment with antiemetics (Ondansetron 4 mg every 8 hours) was started with partial clinical improvement. Amitriptyline 10 mg/day was added with a good clinical response. He did not repeat episodes of vomiting 6 months after starting therapy.

## DISCUSSION

CVS is a functional disorder, described for the first time in 2006, whose diagnostic criteria were defined in the Rome III consensus.<sup>8</sup> In Rome IV, these were modified and the time criterion was specified, so that they are currently defined by the presence of at least 2 episodes of vomiting lasting less than 7 days, in the past 6 months or 3 or more episodes in the past year, during the past 3 months with symptom? onset at least 6 months before.<sup>1,3</sup> This case met these criteria and once other etiologies were excluded, the diagnosis of CVS was made. The intensity of vomiting, as well as its frequency, led to the emergency consultation on multiple occasions.<sup>5</sup> Prior to diagnosis, the patient had more than 10 admissions for parenteral hydration.

The onset of symptoms that were interpreted as biliary affiliation, as well as ultrasound finding of gallstones with elements of acute cholecystitis, justified emergency cholecystectomy. There are no data reporting an association between both pathologies, or which surgical history triggers CVS. However, the persistence of vomiting after surgery forced another etiological cause to be reconsidered. Once the most frequent pathologies are discarded, it is very important to suspect this diagnosis. This entity is a disorder that is usually underdiagnosed.<sup>6,7</sup>

Other diseases associated with CVS have been described. The patient's headache with migraine characteristics supports the idea of this syndrome due to a common pathophysiological mechanism and its relationship with stress.<sup>1,2,4,6,9</sup> Other etiologies which have been related to CVS are irritable bowel syndrome and gastroesophageal reflux disease.<sup>2</sup>

Psychiatric pathologies, such as anxiety, presented by this patient, and depression, are frequently associated with functional digestive disorders, and CVS is no exception.<sup>2</sup> The risk is increased 2.5 times more than the general population. The quality of life of these patients is affected during episodes of vomiting. According to Hasler *et al.*, the presence of psychiatric comorbidities associated with CVS has a negative impact on quality of life and is associated with disability.<sup>6,7</sup> In the reported case, the symptomatic periods had repercussions on the patient's social and working environment.

Within differential diagnoses it is very important to exclude cannabinoid hyperemesis syndrome. Unlike CVS, the latter can present with normal gastric emptying and the absence of psychiatric comorbidities.<sup>6,10</sup> Cannabis use was ruled out in this case.

Diabetes mellitus constitutes a differential diagnosis of CVS that must be actively searched for, given that metabolic imbalance can be the cause of recurrent vomiting. The patient presented this pathology, however, he had excellent control of his glycemia figures, as well as absence of target organ involvement, which removes the connection with vomiting in this case. The presence of diabetes can make management difficult during the period of hyperemesis, due to the possibility of ketosis linked to its pathology.<sup>2,11</sup>

Treatment of CVS involves fluid and electrolyte replacement measures during acute episodes, control of vomiting with antiemetics, and prevention of recurrence.<sup>12</sup> Ondansetron is the first-line drug to control nausea and vomiting, with a maximum dose of 32 mg/day.<sup>1,2,7,12</sup> In those patients who have a partial response to it, Sumatriptan is a valid option for symptomatic control. It is used during the prodromal phase at a dose of 20 mg intranasally or 6 mg subcutaneously. It has been shown that the use of non-steroidal anti-inflammatory drugs or opioids can be beneficial in those patients with CVS who present abdominal pain.<sup>2</sup>

Amitriptyline is the drug of choice for prophylactic treatment. This corresponds to a mixed serotonin and norepinephrine reuptake inhibitor TCA that also interacts with cholinergic and histamine receptors.<sup>7,13</sup> Adverse effects are very frequent, particularly those linked to its anticholinergic action such as dry mouth, constipation, blurred vision and urinary retention. Non-anticholinergic manifestations such as photosensitivity, obstructive jaundice, and stomatitis may also occur.<sup>13</sup> Fortunately, the patient did not present any of these. It has been shown that amitriptyline has greater efficacy compared to Topiramate and Levetiracetam.<sup>2</sup> A randomized clinical trial led by Bagherian *et al.* compared the efficacy of amitriptyline and topiramate in CVS prophylaxis, being the same 52-93% and 38-56%, respectively.<sup>14</sup> Additionally, amitriptyline has beneficial effects for the treatment of migraine.<sup>15</sup>

In order to achieve the neuromodulatory effect and not the antidepressant one, the recommended dose in the SVC is 10 mg/day. The mechanism of action is not dose-dependent, so increases in dose can generate tolerance.<sup>7,15</sup> In the reported case, a good clinical response was achieved without recurrence of vomiting episodes with amitriptyline.

The use of anticonvulsants is a valid option in the absence of response to TCAs.<sup>1,2,7</sup> Single-dose

risperidone, alone or associated with amitriptyline, has been used in cases of refractory CVS due to its antiemetic properties.<sup>2,15</sup>

Non-pharmacological therapies such as meditation, relaxation, gastric electrical stimulation and biofeedback are complementary therapies for symptom control and reduction in the frequency of CVS episodes.<sup>7,13</sup>

More than 6 months after starting treatment with TCAs, the patient did not present any more episodes of nausea or vomiting, with good tolerance and without adverse effects.

## CONCLUSION

CVS is a functional disorder whose diagnosis requires clinical suspicion, as well as the exclusion of organic causes of vomiting. It is a frequently underdiagnosed entity, hence the interest in disseminating it to the medical community. Treatment consists of fluid and electrolyte replacement and antiemetics during episodes of vomiting and the use of TCAs to prevent recurrences, as well as to improve the quality of life of these patients.

### Abbreviations:

5-HT<sub>3</sub>: type 3 serotonin receptor.  
TCA: tricyclic antidepressant.  
CVS: cyclic vomiting syndrome.  
CT: computed tomography.

**Conflicts of interest:** The authors declare that they have no conflicts of interest.

**Sources of funding:** The authors declare they have no financial interests.

## REFERENCES

- Hayes W, VanGilder D, Berendse J, et al. Cyclic vomiting syndrome: diagnostic approach and current management strategies. *Clin Exp Gastroenterol.* 2018; 11: 77-84.
- Shearer J, Luthra P, Ford AC. Cyclic vomiting syndrome: a case series and review of the literature. *Frontline Gastroenterol.* 2018; 9 (1): 2-9.
- Stanghellini V, Chan FK, Hasler WL, et al. Gastrointestinal disorders. *Gastroenterology.* 2016; 150 (6): 1380-92.
- Tamahir AM, Salim A, Abdullah M. Cyclic Vomiting Syndrome: A Case Report and Mini Literature Review. *Cureus.* 2020; 12 (11): e11695.
- Venkatesan T, Tarbell S, Adams K, et al. A survey of emergency department use in patients with cyclic vomiting syndrome. *BMC Emerg Med.* 2010; 10: 4.
- Hasler W, Levinthal D, Tarbell S, et al. Cyclic vomiting syndrome: Pathophysiology, comorbidities, and future research directions. *Neurogastroenterol Motil.* 2019 Jun; 31 (Suppl 2): e13607.
- Venkatesan T, Levinthal D, Tarbell S, 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.
8. Tack J, Talley NJ, Camilleri M, et al. Functional gastroduodenal disorders. *Gastroenterology.* 2006; 130: 1466-79.
  9. Tang C, Dai N. Highlighting the importance of early diagnosis of cyclic vomiting syndrome in adults: A case report. *Medicine.* 2019; 98 (51): e18365.
  10. Burillo G, Hernández I, Isorna M, Hiperemesis por cannabis versus vómitos cíclicos. *Adicciones.* 2021; 33 (4): 377-8.
  11. Ogiso K, Koriyama N, Akao A, et al. Type 1 diabetes complicated with uncontrollable adult cyclic vomiting syndrome: a case report. *J Diabetes Metab Disord.* 2015; 14: 72.
  12. Amy D, Carrie J, Bryant J. Cyclic vomiting syndrome. Treasure Island: StatPearls Publishing LLC, 2022.
  13. Heckroth M, Lockett RT, Moser C, et al. Nausea and Vomiting in 2021: A Comprehensive Update. *J Clin. Gastroenterol.* 2021; 55 (4): 279-99.
  14. Bagherian Z, Yaghini O, Saneian H, et al. Comparison of the Efficacy of Amitriptyline and Topiramate in Prophylaxis of Cyclic Vomiting Syndrome. *Iran J Child Neurol.* 2019; 13(1): 37-44.
  15. Hermus IP, Willems SJ, Bogman AC, et al. Cyclic Vomiting Syndrome: An Update Illustrated by a Case Report. *Prim Care Companion CNS Disord.* 2016; 18(3): 10.4088.

**Correspondence:**

Ignacio Moratorio  
Address: Ing. Garcia de Zuñiga 2315/101,  
CP 11300, Montevideo, Uruguay.  
(+59) 897109598  
E-mail: ignaciomoratorio@gmail.com