

# A Multidimensional Strategy: Ways to Combat Cyclic Vomiting Syndrome with Hiatus Hernia and Gastroesophageal Reflux Disease in a Young Adult Female

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## ABSTRACT

Cyclical vomiting syndrome (CVS) is a chronic idiopathic functional gastrointestinal disorder characterised by intermittent episodes of severe nausea and vomiting with symptoms-free intervals in between. CVS is seen in various age groups with a prevalence of 1.9%. Numerous psychosocial, physical and infectious stressors have been attributed as a trigger of CVS. Often, a co-existing organic and psychiatric comorbidities mask the disorder, and an absence of diagnostic investigation causes a delay in diagnosis and makes it challenging to treat.

## INTRODUCTION

Cyclical vomiting syndrome (CVS) is an idiopathic chronic disorder characterised by recurrent episodes of vomiting and nausea separated by relatively asymptomatic periods. CVS is considered a form of migraine. However, it is also associated with a high incidence of psychiatric comorbidities, such as panic attacks, anxiety and depression both in children and adults. CVS which is more commonly seen in female, is not a rare disorder. However, the etiology behind this syndrome is still unknown. The poor recognition of CVS by clinicians has led to many patients suffered for years. It is vital to identify CVS' patients early, as there are several effective prophylactic and abortive therapies to treat this disorder. Here, we present a case report of a young woman diagnosed with CVS since childhood to highlight the new pharmacology agents and multidisciplinary approach used in managing her case.

## CASE REPORT

An 18-year-old girl was referred to the gastroenterology clinic for unexplained recurrent vomiting and multiple episodes of abdominal pain for ten years. The episodes

usually presented in a stereotypical pattern with sudden onset of nausea and vomiting multiple times, lasting for several days. Sometimes, hospitalisation for supportive measures is required for severe symptoms. In between the attacks, she was perfectly well. She had regular menses and her symptoms were unrelated to her menses. Her first episode started at the age of 8 years old, about 5 months after her younger brother was born, showing a possible relationship. She was admitted for evaluation of recurrent vomiting.

All the blood investigations, including MRI brain and barium study, were normal. She was initially suspected of suffering from anxiety disorder with functional dyspepsia. She was discharged home well with T. Alprazolam, T. Lansoprazole and T. Propranolol as she improved following the treatment. She had similar attacks and had multiple admissions throughout the years. During her childhood hospital admission, she was seen by a child psychiatrist for learning difficulties and later was diagnosed with cyclical vomiting syndrome. She faced significant psychosocial stressors at the age of 8-year-old after she

had her younger brother. She faced sibling rivalry, which was the starting point of her medical condition. Unfortunately, her parents later defaulted the psychiatric appointment and sought treatment from a private hospital. In 2015, she was diagnosed with erosive gastritis from an upper endoscopy at a private hospital. Since then, she was given multiple courses of T.esomeprazole, Syrup Gaviscon, T. Escitalopram and T. Ondansetron as she was treated for anxiety disorder with gastritis.

She had temporary relief with the medication. The symptoms and attacks got worse after she furthered her studies in college. Her most recent endoscopy, which was done during her admission in November 2019, showed Hill Grade II hiatus hernia with Los Angeles Grade C erosive esophagitis. Again, she was discharged home with the same medication but was referred to a gastroenterologist at a university hospital. In March 2020, she had readmission with a similar presentation. She was treated with intravenous Ondansetron 8mg OD, Pantoprazole 40mg BD and T. Alprazolam 0.5mg ON. Her condition did not improve, and T. Aprepitant 125mg OD was prescribed. Soon, her condition improved with this newer drug Aprepitant, and she was discharged home 5days later. The medication dosage was titrated, T. Aprepitant 80mg PRN was given during discharge and symptoms free upon review three months later.

Physical examination revealed no abnormality. On mental status examination, she was well-kempt, cooperative, and a good rapport was established. She answered the questions relevantly and coherently. No psychopathology was elicited from her speech, thought and mood. During her recent visit to the gastroenterology clinic, she had no more recurrent vomiting episodes or abdominal pain after being started on T. Aprepitant 80mg PRN and T Pantoprazole 40mg OD. She was able to get back to college, focus on her studies and lead a better life without frequent hospitalisation. Her final diagnosis upon being discharged was revised to cyclical vomiting syndrome with erosive gastritis.

## DISCUSSION

CVS is a chronic functional gastrointestinal disorder characterised by intermittent episodes of severe nausea and vomiting with symptoms-free intervals in between. The aetiology behind this syndrome is still unknown. A recent population-based study showed that the prevalence of CVS in Canada is 0.7%, in the United Kingdom is 1%, and in the USA is 2%.<sup>1</sup> CVS diagnosis is based on Rome criteria, first developed in 2006 and later revised in 2016.<sup>2</sup> According to the Rome IV criteria, CVS have the following characteristics: Stereotypical episodes of vomiting at least two acute-onset episodes in the past six months, each occurring at least one week apart, and persisting for less than one week. Furthermore, there is an absence of vomiting between episodes, but other milder symptoms can occur between cycles.

Supportive findings include a personal or family history of migraine. The criteria must be fulfilled for the past six months, with symptoms onset at least three months before diagnosis. The syndrome is made of 4 phases: the prodromal phase, vomiting phase, recovery and asymptomatic or inter-episodic phase.<sup>3</sup> Intense nausea, panic symptoms and autonomic symptoms such as diarrhoea, cold and hot flashes, and profuse sweating usually occur in the prodromal phase. This is later accompanied by an acute emetic phase where the patient will suffer from severe vomiting and retching. Vomiting episodes can vary from 1 to 6 times/hour, and the retching often persists despite emptying the stomach.

About 70% of the patients can present with abdominal pain. As the time passes from hours to days, patients will slowly enter the recovery phase, once they are able to resume eating and return to their baseline. The diagnosis of CVS remains a challenge, as there are no specific diagnostic biomarkers in CVS, making it largely one of exclusion. Certain presentations of patients may require the physician to proceed with laboratory investigations, including metabolic tests and imaging such as abdomen and pelvis ultrasound, intestinal magnetic resonance and brain imaging. Besides, an esophagogastroduodenoscopy may be needed, following repeated vomiting, as

hematemesis may occur.<sup>4</sup> Yet, all these modalities may only help the clinician reach the diagnosis rather than directly pointing towards it. To achieve a great outcome, the treatment plan for this syndrome should be comprehensive. In 2008, the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) consensus had proposed the “five strategies” plan to combat CVS based on a review of medical literature and expert opinion. It is currently considered to be the best approach to treat CVS. This treatment plan includes prophylactic pharmacology, acute phase therapy, supportive care and general family support.<sup>5</sup> As for abortive medication, Sumatriptan, a serotonin agonist, is found to be effective, especially during the prodrome phase. It's best given within 30-45min of the onset of vomiting as the efficacy seems to diminish after the first 60min.<sup>6</sup> On the other hand, Ondansetron, the 5-hydroxytryptamine type 3 receptor antagonist routinely used for patients with chemotherapy-induced nausea and vomiting, is recommended as a first-line abortive agent during an acute attack by American Neurogastroenterology and Motility Society (ANMS) and Cyclic Vomiting Syndrome Association (CVSA) guideline.

In a refractory case, a neurokinin-1 (NK1) receptor antagonist - Aprepitant is a novel and effective choice that can be used both as abortive therapy and prophylactic therapy.<sup>7</sup> It primarily acts at the brainstem nucleus tractus solitarius exerting anti-vomiting effect. Besides, it has a low side effect profile and has the properties of antidepressant and anxiolytic. Cristofori et al. had retrospectively review sixteen CVS children treated prophylactically with Aprepitant and found that thirteen children (81%) achieved either complete (19%) or partial (62%) clinical response at 12-month analysis.<sup>8</sup> Aprepitant appears to effectively decrease the duration and intensity of CVS when given before the beginning of the emetic phase.<sup>8</sup>

Supportive care, including providing a less stimulating (e.g., dark, quiet) environment, giving fluids, electrolytes, and energy replacement, providing adequate analgesia and antiemetics, can be done in the acute phase.<sup>5</sup> As for prophylactic therapy, Amitriptyline (AT), a tricyclic antidepressant, stands as the first-line prophylactic medication. <sup>(10)</sup> It was proved across many studies that AT

decreases the frequency, duration and severity of CVS symptoms. An open-label study involving 46 patients by Hejazi et al. <sup>1</sup> showed a significant reduction in the duration of a CVS episode from 6 to 2 days, in the number of ED visits/hospitalisations from 15 to 3.3 and in the number of CVS episodes from 17 to 3 with AT.<sup>9</sup> Namin F et al. <sup>1</sup> in an observational study reported that out of 24 patients who were given AT for at least three months 26% had complete remission of the symptoms while 93% had a reduction in symptoms measured by a visual analogue scale.<sup>10</sup> Alternative prophylactic medication such as Topiramate can also be used as a single prophylactic agent or combined with other agents, such as amitriptyline in treating CVS. In cases where the standard prophylactic therapy fails, anticonvulsants such as Zonisamide and Levetiracetam are also found effective.

The non-pharmacological aspect should be given equal importance in managing CVS. Educating the patient on avoiding the triggers during the good phase and lifestyle modifications such as regular exercise, proper sleep hygiene, and good hydration is the key to effective management. Mind-body intervention such as meditation and relaxation combined with cognitive behavioural therapy will further enhance the treatment's success.<sup>6</sup> Limitation in this case report is that the patient did not undergo Gastrointestinal (GI) motility testing due to the patient's and family are not keen.

#### **CONFLICT OF INTEREST**

No potential conflict of interest relevant to this article was reported.

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