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CASE REPORT

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## The Challenges of Cyclic Vomiting Syndrome in Type 1 Diabetic Adult: A Multidisciplinary Approach

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### ABSTRACT

The following case describes the presentation of Cyclic Vomiting Syndrome and the challenges of making an accurate diagnosis and instituting effective treatment in diabetic patients. The overlap of gastric symptoms of nausea, vomiting and abdominal pain in diabetics between the diagnosis of gastroparesis and cyclic vomiting syndrome increases the difficulty of making a correct diagnosis. This particular case emphasizes the importance of recognizing the symptoms of this entity at an early stage. A multidisciplinary approach involving a team of gastroenterologist, psychiatrist, psychologist, primary care physician, nursing support, and social worker is needed to prevent attacks and keep the patient at home rather than have dehydration and pain sending the patient to a more anxiety generating environment such as the Emergency Room.<sup>1,2,22</sup>

### BACKGROUND INFORMATION

Cyclic vomiting syndrome (CVS) in adults is an episodic disorder characterized by highly intense nausea and vomiting presenting in a stereotypical pattern usually accompanied by severe abdominal pain lasting from hours to days, separated by intervals of days to weeks which are free of symptoms.

This case portrays the challenges from diagnosis to treatment of CVS in diabetics where our diagnostic tendencies favor gastroparesis whenever we are confronted with a history of frequent vomiting in a diabetic.<sup>18,19</sup> The case also emphasizes the importance of gastric emptying studies.<sup>2,5,11,12,15</sup>

### CASE PRESENTATION

A 28 year old Hispanic female presented to the emergency room with a chief complaint of nausea, vomiting and abdominal pain.

She had a 5 year history of recurrent episodes of uncontrolled emesis, 10-20 a day described as clear, bilious and sometimes with coffee-ground appearance, but no food content, as well as epigastric pain which radiated to the back. Episodes are predictable and accompanied by a sense of anxiety. Onset is usually at night or early morning. The episodes generally end abruptly after 4-5 days and then are followed by a period of a week to 1-2 months free of symptoms. Treatment acutely has included IV fluids, benzodiazepines (Lorazepam) for sedation, antiemetics, proton pump inhibitors, and opiates to treat the severe pain.

She reported that anticipating her next episode is definitely the worst of her fears. In the last 3 years she has had a total of fifty Emergency Department visits or hospitalizations.

### Medical history remarkable for:

Type 1 DM at age 21, hypertension at age 24, cyclic vomiting syndrome at age 23, miscarriage in 2007, adjustment disorder and unresolved grief. No surgeries. Both parents deceased due to complications of type 2 diabetes.

Allergies to vicodin and metoclopramide (dystonic reaction).

### Medications at home:

Lisinopril, Insulin glargine, clonidine, phenergan, amlodipine, amitriptyline, clonazepam, ondansetron, pantoprazole.

### Physical exam:

She was in moderate distress lying in bed with a container moistened by clear vomit.

Mental status: Alert and awake. Able to give some history in between bouts of emesis. Dry mucous membranes; lungs clear to auscultation bilaterally; tachycardic heart sounds; no murmur; bowel sounds present. She had tenderness to palpation in the epigastric area with no rebound and no organomegaly.

### Her labs on admission were remarkable for

Blood glucose level 500 mg/dl.

CBC Hemoglobin: 11mg/dl. Creatinine 1.9mg/dl. Normal electrolytes.

Urine: microscopic hematuria.

Hemoglobin A1C 11.0

### Assessment:

This is a patient with long standing type 1 DM, poorly controlled as demonstrated by her elevated A1C levels, 2 gastric emptying studies using an isotope labeled egg meal for 4 hours duration and they were found to be within normal limits or on the rapid side of normal. This provided final support for the diagnosis of cyclic vomiting syndrome by separating it from slow gastric emptying that would be present in gastroparesis.

### Outcome:

Latest discharges have shown good response to benzodiazepines. Unfortunately, tricyclics (TCAs) have not been able to achieve prevention of relapses.

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Options for long term prevention in non-responders to tricyclic antidepressants include levetiracetam (Keppra), propranolol, ciproheptadine and Sumatriptan (even nasally), the latter being particularly valuable where migraine headaches remain in the background.<sup>2,12,13,14</sup>

Treatment goals are to: Prevent episodes, abort episodes, terminate episodes using sedation until cycle passes, limited re-feeding to avoid triggering relapse,<sup>1</sup> optimal control of blood glucose to minimize relapses and co-management with psychiatry and psychology if indicated which was needed in this patient since anxiety stress and panic disorders are known risk factors as well as depression.

**DISCUSSION**

Cyclic vomiting syndrome (CVS), in adults, is an episodic disorder characterized by highly intense nausea and vomiting presenting in a stereotypical pattern usually accompanied by severe abdominal pain, lasting from hours to days, separated by symptom free periods.<sup>1,2</sup>

Cases have been reported since 1806 in France by Dr W Herberden<sup>3,5</sup> and in 1882 in England by Dr Gee.<sup>4,5</sup> Initially thought to be limited to children, more recently the syndrome has been described in adults<sup>2,4,6</sup> and now it is being recognized more in adults than the pediatric age group. In 2006 formal diagnostic criteria were adopted by the ROME III classification of functional gastrointestinal (GI) disorders.<sup>2,5,6</sup>

Diagnostic criteria. Must include all of the following:

1. Stereotypical episodes of vomiting regarding onset(acute) and duration (less than a week)
2. Three or more discrete episodes in the prior year.
3. Absence of nausea and vomiting between episodes

Supportive criterion:

History or family history of migraine headaches.<sup>6</sup>

CVS is a clinical diagnosis, often challenging because there is no specific or typical laboratory test, imaging study or other diagnostic tool. It is essentially a diagnosis based on the classic symptom pattern of presentation as well as exclusion of possible other diagnosis. It is classified in the category of “functional”,<sup>1,2,7</sup> and it is best recognized and appropriately treated based on a very typical and predictable history and clinical presentation.

**Phases of CVS:**

**Inter episodic:** “symptom free”.

**Prodromal:** sense of oncoming episode, still able to intake food and liquids. Principal symptoms are nausea, sweating, abdominal pain, heat and cold in tolerance, urge to defecate, food aversion, irritability or panic. (Minutes to hours).

**Vomiting:** intense, persistent nausea, vomiting, retching and with severe abdominal pain and lethargy. (Hours to days).

**Recovery:** begins as soon nausea remits and ends when the patient recovers appetite, strength, and returns to daily functioning.<sup>1,2,8,16</sup>

Potential triggers for acute episodes include infections, psychological stress (positives and negatives), motion sickness, sleep deprivation, physical exhaustion, migraine headaches, menses, high blood glucose levels and certain foods (chocolate, cheese, red wine, monosodium glutamate).<sup>18</sup>

Common co-morbidities in CVS are migraine headaches, Psychiatric diseases (Anxiety and depression), chronic marijuana use, autonomic neuropathy disease, irritable bowel syndrome and diabetes mellitus. About 12% to 15% of CVS patients have diabetes, more than the prevalence of diabetes in the general population which is approximately 8%. This increased incidence raises the possibility that fluctuating and specially very high glucose levels for example more 250 mg %, may provoke a CVS vomiting and pain cycle.<sup>1,2,8,9,14,20</sup>

Anxiety is surprisingly prevalent in adult patients.<sup>5,7,14</sup> It seems to have multiple sources: (a) the burden of illness, including physical suffering and the economic and marital stress caused by it; (b) anticipatory anxiety for the episode-to-come; (c) a established background of anxiety and depression preceding the CVS onset, and (d) anxiety originating from psychological trauma experienced during childhood and young adulthood or prior to the onset of CVS in a subset.<sup>5,7</sup>

Anxiety promotes nausea and nausea which in turn leads to more anxiety as a result episodes tends to become more frequent and more disabling.<sup>1</sup> Sleep becomes poor. Their attendance at work or school falls off.<sup>5</sup> Deterioration in the course of CVS is characterized by coalescence of attacks, increasingly frequent episodes and more anxiety, dyspepsia and nausea between episodes. Abdominal pain control can raise questions of “narcotic seeking” behavior by the Emergency Department staff. Complete coalescence of episodes causes the patient to be sick for weeks or months at a time and sick more than well which then can make distinguishing CVS from gastroparesis very difficult based on symptoms. Here the gastric emptying study is a key. It actually is rapid in over 60% of patients and normal in the others where gastric emptying is always slow or delayed in gastroparesis. The gastric emptying study should be conducted between acute attacks and away from narcotic use or marijuana smoking, both of which can delay gastric emptying.<sup>5,11,17,18</sup>

**Treatment**

The treatment goals and target vary accordingly with the clinical phase:

**Inter episodic:** 1. Prevent episode by avoiding of trigger events, 2. prophylactic tricyclic antidepressants, 3. Cyproheptadine , propranolol, sumatriptan (Imitrex) can be helpful in the setting of migraine, 4. Acute anxiety prophylaxis with Lorazepam.

**Prodromal:** Abort episodes with antiemetics like ondansetron, promethazine or prochlorperazine, anxiolytics like lorazepam or alprazolam and pain management with ibuprofen, tramadol, dilaudid, oxycodone if needed. Hot showers and hot baths have a very specific role in reducing the abdominal pain, nausea and vomiting and is an important “clinic pearl” to elicit in the history.

**Vomiting:** Sedate with IV Lorazepam until episode passes,

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treat dehydration with IV fluids, nausea with ondansetron, and opiates for pain. In addition sedation with diphenhydramine can be included. Sumatriptan can be used if migraine headaches present.

**Recovery:** Limited re-feeding without causing relapse. Resume prophylactic medication with slowly increasing doses of tricyclic at night as soon as possible. Dose levels as high as 200 mg or more may be required based on tolerance and efficacy.<sup>1,2,5,8,16</sup>

Treatment with tricyclic antidepressants for prevention and attenuation has a less impressive response in patients with co existing disorders like depression and anxiety, who continue to smoke marijuana and/or are taking chronic narcotics for pain.<sup>8</sup>

**FOLLOW UP**

Adding to the challenge is how to explain to an already frustrated patient that his/her emotions play a role in the syndrome. In this case although depression was not acknowledged in the beginning, it ended up being included in her diagnosis after proper mental evaluation by Psychiatry and obvious triggers were discovered. (Death of parents and a miscarriage right before the onset of the syndrome). It is vital that we transmit this message to the patient: Anxiety is definitely a trigger and therefore, by addressing it the effectiveness of the tricyclics in reducing the frequency and intensity of the cycles is enhanced.

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