

Adult Cyclic Vomiting Syndrome Is Easy to Miss

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BOSTON — Cyclic vomiting syndrome in adults often goes unrecognized for years after onset, despite its severe and disabling consequences.

The disorder may be the cause of repeat visits to emergency departments, unnecessary surgeries and diagnostic tests, and substance abuse, according to participants at the first-ever symposium devoted to cyclic vomiting syndrome (CVS) in adults. The gathering was held as a satellite meeting following a meeting on neurogastroenterology and motility.

Diagnosis of CVS in adults is complicated by the variability in age of onset and pattern of symptoms. The result is that the average delay in making the diagnosis is 8 years from the time symptoms first appear, noted Dr. B. U.K. Li, director of the Center for CVS at the Medical College of Wisconsin, Milwaukee, in a presentation at the meeting.

"Where were we? How did we miss these folks?" Dr. Richard McCallum of the Kansas University Medical Center, Kansas City, rhetorically asked the audience, composed of physicians, patients, and family members.

As the director of the first center for CVS in adults, Dr. McCallum said, "We're getting a continued trickle of patients coming to us, and an avalanche of phone calls from patients and physicians from around the world."

According to the Rome 3 criteria H1b, the definition of CVS is two or more periods of intense nausea or unremitting vomiting or retching lasting hours to days,

with a return to the usual state of health lasting weeks to months (J. Gastro. Liver Dis. 2006;15:237-41). In its mildest form, the symptoms of CVS do not interfere with a patient's ability to work or attend school, said Dr. David Fleisher of the University of Missouri, Columbia, who has studied 41 adults with CVS.

He found that about 8% of his sample had mild symptoms, 44% had moderate symptoms that caused them to worry about their ability to continue work or school, and about 49% had incapacitating symptoms so severe that they were sick more often than they were well.

Some of these patients experienced eight or more vomiting episodes per hour for months on end, leading in some cases to more than 100 visits to the emergency department or hospitalizations. As CVS progresses, episodes may become more frequent with less time for recovery, a process Dr. Fleisher terms "coalescence."

When rushed to the emergency department during the emetic phase, CVS patients can present with blood in the vomitus due to prolapse gastropathy or Mallory-Weiss tears resulting from forceful heaves, erosive esophagitis, and aspiration. Dehydration and electrolyte imbalance, particularly hypokalemia, may accompany the GI symptoms.

Patients often experience intense abdominal pain, and may demand narcotics; they may show signs of narcotic depen-

dence. Tooth decay can be evident, and patients may describe chronic weight loss, Dr. Fleisher said.

Patients also may show signs of a hyperadrenergic state, including low-grade fever, rapid pulse, and hypertension. Neu-

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trophilia without bandemia, accompanied by abdominal pain and vomiting, may be misdiagnosed as pancreatitis, peptic ulcer, appendicitis, or pyelonephritis. The periodicity of attacks, with or without hypertension, may lead to confusion and give the impression of porphyria, pheochromocytoma, abdominal epilepsy, intermittent small bowel obstruction, or endometriosis.

Patients also may present with unusual behaviors and mental states that compound the difficulty of identifying CVS. Normally pleasant and affable patients may become irritable and verbally abusive, demanding medications. Patients may describe thirst so intense that they drink surreptitiously from toilet bowls. They may engage in a guzzle-and-vomit sequence that can be mistaken for bulimia, and which may actually be explained by the transient relief provided by sudden emptying of the stomach.

Other patients may ask for repeated hot showers or baths. Some patients may appear so immobile that it is difficult to establish whether they are asleep or awake; they also may withdraw from social contact, a frightening condition Dr. Fleisher describes as "conscious coma."



CVS patients often undergo batteries of tests, including upper GI series, abdominal ultrasound and CT scan, colonoscopy, barium enema, endoscopy, MRI of the head, sinus radiography, EEG, and lab work, usually with negative results.

In Dr. Fleisher's series, the 41 patients underwent almost 300 diagnostic studies—none of which were indicative of an organic etiology for CVS. Recent findings suggest that about 75% of patients with CVS show rapid gastric emptying on electrogastrograms, and this may help distinguish CVS from other vomiting disorders (Neurogastroenterol. Motil. 2006;18:728 [abstract 200]).

Unnecessary surgeries are also common. Of the 41 patients in the series, 10 had undergone cholecystectomies, 2 had appendectomies, 5 had laparoscopies, 1 had a hysterectomy, and others had undergone other GI procedures. None of these procedures relieved the CVS symptoms.

Part of the problem is the lack of continuity of care for these patients, especially those who present repeatedly to hospital emergency departments. Dr. Fleisher suggests that more CVS centers should be created and staffed by two to three physicians available 24/7, as well as by nurses and mental health professionals. A patient can be managed routinely by his primary care physician, and then referred when necessary to a CVS center cognizant of his history, he added.

The Cyclic Vomiting Syndrome Association (www.cvsaonline.org) is establishing a referral network and provides resources for physicians who want to learn more about the syndrome.

Knowledge, Patience Key to Managing the Four Phases of Cyclic Vomiting Syndrome

A physician must be knowledgeable, accessible, patient, nonjudgmental, and quick to respond when treating adults with cyclic vomiting syndrome, Dr. Fleisher said, and follow a rational treatment plan, tailored to the phase of the disease, that includes sedation when symptoms rage uncontrollably.

The CVS cycle has four phases, said Dr. Fleisher, who has treated more than 350 pediatric and adult CVS patients at the University of Missouri Hospital and Clinics, Columbia. The time between episodes, when the patient is feeling well, can be considered the first phase. The goal in this phase is to prevent a CVS episode by recognizing and controlling triggers, such as menstruation, noxious stress, pleasant excitement, fatigue, or infection. Some patients have interepisodic dyspeptic nausea and abdominal discomfort, especially in the mornings, and they may respond to proton-pump inhibitors.

The physician should help the patient regain a sense of being in control, rather than being at the mercy of CVS symptoms; this can be critical in determining overall treatment success, he said.

Dr. Fleisher considers CVS to be a manifestation of migraine diathesis in some patients. In a group of 41 adults with CVS, 70% had migraines during or between episodes, and 57% had first- and/or second-degree relatives with migraines. For these patients, migraine prophylaxis is essential to prevent CVS symptoms.

For two-thirds of Dr. Fleisher's group, severe anxiety and panic attacks triggered CVS episodes, and the panic symptoms persisted for hours or days. He likens

the symptoms to those of an "adrenergic storm" seen in patients with pheochromocytoma. Patients begin to fall into a vicious cycle of anticipatory anxiety, whereby the worry about having a CVS episode increases the likelihood of another attack.

Some CVS patients have a propensity to both migraines and anxiety/panic attacks. A careful medical history can help physicians recognize the pathogenic factors specific for each patient, leading to an appropriate preventive strategy.

In the prodromal phase, the physician and patient have the chance to abort the emetic phase. In Dr. Fleisher's group, 93% had recognizable prodromes; common symptoms included nausea, sweating, epigastric pain or pressure, fatigue or weakness, feeling hot or cold, cramping urge to defecate, abdominal pain, shivering or shakiness, insomnia, food aversion, palpitations, irritability, and panic.

Depending on the symptom, appropriate medications during the prodrome include lorazepam, alprazolam, and/or ondansetron orally or sublingually for nausea, analgesics for abdominal pain, antianxiety medications for anxiety, and a triptan for headaches. Sleep may also be beneficial.

During the emetic phase, the goal is to rapidly terminate the episode, preferably within 1 hour of onset. In a sample of 39 adults with CVS, more than half had vomiting episodes lasting 3 days or more. Steps to take include prevention or correction of dehydration with IV fluids, and IV administration of antiemetics, antianxiolytic agents, and H₂-receptor blockers or

proton-pump inhibitors. In some cases, IV opiates are necessary for pain control. Patients should be checked for electrolyte depletion, tetany, hematemesis, and secretion of inappropriate antidiuretic hormone.

If the CVS episode cannot be terminated, Dr. Fleisher recommends sedating the patient in a dimly lit and quiet room until the episode passes. "A CVS patient needs to know there is an escape hatch that gets them out of their misery. Without that, the more they will suffer and the more they will coalesce," Dr. Fleisher said, referring to the process in which CVS episodes become more and more frequent. He recommends chlorpromazine (0.5-1.0 mg/kg) plus diphenhydramine (0.5-1.0 mg/kg) in normal saline over 15 minutes, which can be repeated as often as every 3-4 hours if needed.

The duration of the recovery period reflects the adequacy of management of the emetic phase. Patients with severe fluid or electrolyte deficits will have a more difficult and prolonged recovery. Some patients can tolerate a normal diet soon after the emetic phase passes, while others will tolerate only clear liquids.

"Long waits in emergency rooms, encounters with caregivers who are unfamiliar with CVS, receiving implausible diagnoses, the repetition of unrewarding diagnostic procedures, and stopgap intravenous hydration followed by being sent home still sick are common experiences that reinforce patients' feelings of being out of control of an illness that no one understands or can treat," Dr. Fleisher wrote in a 2005 report on the 41 patients (see www.biomedcentral.com/1741-7015/3/20).