CHALLENGING CASE: CHRONIC DISEASE—DEVELOPMENTAL AND BEHAVIORAL IMPLICATIONS

Cyclic Vomiting*

CASE

Denise is a 10-year-old girl who was admitted to the hospital for treatment of dehydration secondary to severe vomiting for 2 days. She was unable to retain any liquids. This was her 62nd admission for similar symptoms. These began when she was 5 years old. There was no family history of relatives with similar symptoms, but a paternal grandmother had severe migraine episodes for much of her life. Denise’s parents were unable to determine what triggered Denise’s vomiting episodes. At various times, they had restricted certain foods, focused on more regular sleep times for her, and assessed possible stressors in school, but the episodes seemed to occur at random times. The family lived on a farm, and their primary product was hogs. Denise was the second of four children. She was doing well in the fifth grade and was active in 4-H and in Sunday school. There were four living grandparents nearby, as well as many aunts, uncles, and cousins. There were frequent family get-togethers. At physical examination, Denise was irritable, spoke in monosyllables, and preferred to remain curled in a fetal position with her eyes closed. Her temperature was 98.8°F; her pulse was 120 beats per minute; her respiratory rate was 20; and her blood pressure was 85/60 mm Hg. Her eyes were slightly sunken. Her mouth was dry, and her skin appeared dry. Intravenous fluids were begun. After 24 hours, Denise was able to retain popsicles and sips of water. After 48 hours, she was ravenously hungry and was eating solids without difficulty. Her personality had changed dramatically. She was talkative, she laughed frequently, and she was discharged to home.

Index terms: child, cyclic vomiting syndrome.

Dr. Martin T. Stein

Children and adolescents with recurrent episodes of vomiting without an apparent etiology are not seen frequently by general pediatricians. Hospital-based behavioral pediatricians might have more experience with this entity. A recent epidemiologic study in Scotland suggests a higher than expected prevalence of chronic cyclic vomiting syndrome (CVS)—1.9%.1 I selected this case because it represents a situation that straddles the boundary between clearly defined organic disease and a psychosocial-behavioral entity. An earlier report in the Journal’s Challenging Case series—a child with severe school refusal and emotional lability subsequently found to have a brain tumor—illustrates this phenomenon.2 These are the cases that challenge the clinical skills of pediatricians, psychologists, and psychiatrists. They are especially challenging to medical doctors trained to diagnose disorders manifested by symptoms that express interrelationships between mind and body.

I asked three physicians trained as pediatricians to comment on this case. They represent subspecialties that bring different points of view to the evaluation process. Richard M. Katz, M.D., is Assistant Professor of Pediatrics at The Johns Hopkins University School of Medicine. He is a pediatric gastroenterologist with an active clinical, teaching, and research program who directs a program for the evaluation and treatment of children with feeding disorders. Michael S. Jellinek, M.D., is Professor of Pediatrics and Psychiatry at Harvard Medical School. His scholarly writing effectively bridges the language and clinical perspectives of pediatrics and psychiatry. Recently, Dr. Jellinek was instrumental in the development of a practical office-based screening test for behavioral problems seen by pediatricians in primary care practice. Karen Olness, M.D., is Professor of Pediatrics at Case Western Reserve University School of Medicine. She has contributed significantly to our understanding and use of various forms of hypnotherapy and other methods of behavior modification in pediatric practice. Dr. Olness contributed this challenging case.

References


Dr. Richard M. Katz

The first description of fitful or cyclic vomiting is now more than 100 years old, but our understanding and interpretation of the signs and symptoms of this debilitating, complex, and confusing disease entity have not greatly advanced. CVS was first described by Samuel Gee in England in 1882, and his original description is just as apt today as it was then: "These
cases seem to be all of the same kind, there being fits of vomiting which recur after intervals of uncertain length. The intervals themselves are free from signs of disease. The vomit continues for a few hours or days. When it has been severe, the patients are left much exhausted.1

CVS is defined by current convention as having “essential and supportive” criteria.2 Essential criteria include recurrent, severe, discrete episodes of vomiting, with varying intervals of normal health between episodes. The duration of vomiting episodes ranges from hours to days, and no apparent cause of vomiting can be found. Supportive criteria require a stereotypical pattern of vomiting, with each episode similar within individuals as to time of onset, intensity, duration, frequency, and associated signs and symptoms. These episodes are self-limited and are associated with symptoms of nausea, headache, motion sickness, abdominal pain, and photophobia. Also associated with CVS are fever, pallor, diarrhea, dehydration, excess salivation, and social withdrawal.

CVS, which seems to be the cause of Denise’s recurrent hospitalizations, is clearly a disease process that can be established only after exclusion of identifiable causes of vomiting. Vomiting is a nonspecific sign that can result from a disorder of any major organ system. Assessment of any individual with recurrent vomiting requires specific diagnostic testing to ensure that underlying, identifiable causes of cyclic patterns of vomiting can be diagnosed. Many conditions that are difficult to distinguish from CVS can be life threatening if diagnosis is delayed or missed. Therefore, the differential diagnosis of vomiting must be carefully evaluated in each patient presenting with recurrent, prolonged, or chronic vomiting to rule out identifiable causes before a diagnosis of CVS can be entertained.

Gastrointestinal obstruction is the most immediately dangerous condition associated with emesis and should always be evaluated as a possible cause of recurring vomiting. Vomiting, either bilious in nature or not, is associated with malrotations, internal hernias, webs, atresias, and intussusception. Superior mesenteric artery syndrome, peptic ulcer disease, gastritis, esophagitis, and upper gastrointestinal tract motility disorders can present with recurring emesis. Parasitic disease, such as those caused by Giardia, must also be considered in the differential diagnosis of chronic vomiting. Inflammatory bowel disease, pancreatic disease, and celiac disease might also have frequent vomiting as a sign of presentation. Inborn errors of metabolism present with vomiting as a primary manifestation of enzymatic defect. Emesis, which might be recurrent, is often the first clue of urea cycle defects, such as ornithine transcarbamylase deficiency; of organic acidemias, including methylmalonic acidemia; of fatty acid oxidation defects, including medium-chain acyl-CoA dehydrogenase deficiencies; of disorders of gluconeogenesis (pyruvate carboxylase deficiency), as well as such entities as hereditary fructose intolerance and porphyria. Central nervous system involvement in the differential diagnosis of CVS includes all aspects of the function of the brain and spinal cord. Intracranial mass lesions causing increased intracranial pressure or direct invasion of the emetic control centers of the brain are often insidious, and it is not unusual for gastroenterologists to make the diagnosis on the basis of history, examination, and imaging studies. Frequently, seizure disorders are the first suspects when recurrent vomiting is the primary complaint. It is also well established that migraine is one of the disorders presenting as CVS.

The absence of a defined etiology for CVS naturally hinders definitive therapy for individuals, and no clinical trials of pharmacologic agents for relief of nausea and vomiting in CVS have yet been published. The overall goals of treatment must be to ameliorate or interrupt symptoms when they occur, to abort episodes before they occur, and to prevent future episodes. Therapeutic approaches to patients afflicted with the intense nausea and vomiting of CVS should be aggressive and intensive to provide relief as rapidly as possible. The initial treatment must ensure that the patient is stable from a cardiorespiratory perspective. Hydration must be maintained throughout the episode, and, often, intravenous therapy should be instituted early in the course of the event. Oral feedings should be discontinued to minimize vomiting, but case reports indicate that some patients prefer to consume large volumes of liquids during an event (the precise mechanism is unknown, but presumably vomiting might temporarily decrease nausea).3 Metabolic disturbances such as acidosis, hypoglycemia, or electrolyte abnormalities should be corrected rapidly; they might require infusions of 10% dextrose solutions at 1.25 × to 2.00 × the maintenance level, especially if a metabolic abnormality is suspected.

Pharmacologic therapy should include antiemetic agents. Commonly used agents have included chlorpromazine, butyrophenones (droperidol), and benzamides such as metoclopramide and trimethobenzamide. Serotonin (5HT3)-receptor antagonists such as ondansetron have gained considerable favor as antiemetics for CVS. Often, these agents are used in combination with anxiolytics such as lorazepam. A recent article reported the use of parenteral ketorolac as an effective agent in limiting severity and aborting an event of CVS. This suggests a new category of possible etiologies of CVS, i.e., disorders of prosta glandin release.4 Therapeutic goals must also include prophylaxis for future events. Additional classes of pharmacologic agents have been tried for both the acute phase of illness and to prevent recurrences. Agents such as amitriptyline, propranolol, atenolol, and anticonvulsants including phenytoins and barbiturates have been used for years to treat presumed CVS and/or psychiatric causes of CVS. Most recently, trials (uncontrolled) of a motilin agonist (erythromycin9) attempted to abort CVS attacks; erythromycin showed some promise in preventing recurrence in some patients. Finally, some families with CVS patients use homeopathic medications and megavitamins, but no scientific data are available to support claims of effectiveness.
CVS can cause much suffering for children and their families. Although CVS was first described more than a century ago, its pathogenesis and treatment remain elusive. Because the diagnosis requires exclusion of other disorders (such as a central nervous system tumor or metabolic, endocrine, or specific gastrointestinal structural or inflammatory lesions), the child with CVS typically has endured numerous laboratory and radiographic studies, all with negative findings. During episodes, the child often becomes acutely dehydrated and frighteningly ill. Denise and her family, long before the 62nd episode described above, have no doubt been stressed, disappointed, and possibly angry about the pediatrician’s inability to cure her illness.

The pediatrician not only faces personal frustration but must also help the family and child cope with their own helplessness and, at times, despair, while still maintaining a strong alliance with them. Without this sense of trust, the family is likely to “doctor shop” and thus expose Denise to unnecessary procedures, such as repeated endoscopies or even laparotomy. Families are often greatly relieved when the pediatrician identifies this well-accepted disorder and reassures them that their child has no life-threatening or progressive disease. The pediatrician might draw an analogy to other episodic conditions, such as headache, for which no clear organic cause can be identified but which are not alarming. The pediatrician can then help the family to design a collaborative strategy for responding to future episodes that will minimize delay and expedite antiemetic and rehydration treatment.

Given the morbidity and cost associated with CVS, a psychiatric assessment for emotional triggers for CVS, such as depression, anxiety, or trauma, and the child’s interepisode functioning might well be warranted. In many cases, there is an identifiable trigger for the episodes, often emotional excitement or distress. Although Denise’s family did not observe any pattern to her illness, one could suggest that both Denise and her parents keep diaries of the antecedents, symptoms, and consequences of her episodes. These might reveal subtle precipitants, maladaptive responses, and minor symptoms that had gone unnoticed. A psychogenic etiology, even if quite plausible, should not preclude ongoing attention to organic etiologies that might be synergistic and not evident early in the course, e.g., inflammatory bowel disease. If the assessment of triggers indicates a tendency toward anxiety, one could attempt relaxation training, perhaps augmented with biofeedback, on the premise that raising the child’s threshold for physiologic arousal could reduce the frequency or severity of episodes. If a specific trigger can be identified, a desensitization paradigm might be useful, by analogy with behavioral treatment of specific phobias.

Although not described in this case history, chronic or severe CVS can bring a host of secondary risks: major restructuring of family life in response to the perceived needs of the ill child, an immature or too intense parent-child relationship, and “special status” for the child whom the parents might view as vulnerable and in need of protection. In Denise’s case, if this syndrome continues as she enters puberty, the secondary consequences of her illness might limit peer relationships, lower self-esteem, and compromise her ability to separate and individuate from her parents as an adolescent. If CVS begins to impair Denise’s development, family and/or individual psychotherapy might be helpful.

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Children and adolescents with CVS describe the nausea as unbearable. Because repeated vomiting might lead to peptic esophagitis, they often drink large amounts of water during episodes to dilute the acid and bile and make vomiting episodes less painful. Often, children with CVS describe abdominal pain, diarrhea, headaches, chills, and fever. They often have low-grade fever, hypertension, and flushing during episodes. Most children demonstrate marked personality and behavioral changes during episodes, with regressive behavior, many demands, and moaning with discomfort. Only sleep seems to bring relief, but these children will awaken from sleep with more vomiting.2

The differential diagnosis of CVS is extensive, although many diagnoses can be ruled out by history or laboratory findings. Life-threatening conditions, such as bowel obstruction, intermittent volvulus associated with malrotation, internal hernias, and intestinal lymphangiomas, can present with cyclic vomiting episodes. Pancreatitis might also begin with CVS-like symptoms, although they usually do not relent. Chronic intestinal pseudo-obstruction can cause intermittent vomiting, as can obstructive urolologic disease. It is important to check the urinary tract in the evaluation of CVS. Increased intracranial pressure and/or focal central nervous system lesions and family dysautonomia also frequently present with intermittent vomiting.

Several inborn errors of metabolism are manifested by vomiting. These include organic acidurias, fatty acid oxidation defects, disorders of carbohydrate metabolism, and more frequently, disorders of amino acid metabolism. The patient described in this case had a urea cycle defect, ornithine transcarbamylase deficiency. This was relatively easily controlled by a low-protein diet; vomiting recurred only if she breached the diet. I have had referred to me 17 children with years of CVS history who turned out to have a urea cycle defect. Several had experienced prolonged hospitalizations on child psychiatric units.

I have also seen children and adolescents with CVS for whom there was no biologic explanation after years of diagnosis. Among such children, there is often a strong family history of migraine, seizures, or allergies. I think that a failure to identify a precise cause for CVS symptoms reflects our inadequacy in diagnostics rather than a psychologic diagnosis. Most families with CVS or any other chronic illness will have secondary psychologic issues. Often, they perceive themselves as misguided and powerless. Individual or group psychotherapy might be helpful. Fortunately for families with CVS, there is now an active national organization that is on the Internet (http://ezinfo.ucs.indiana.edu/~jdbickel/cvs.html). The mailing address is Cyclic Vomiting Syndrome Association (CVSA), 13180 Caroline Court, Elm Grove, WI 53122. The e-mail address is kadows@post.its.mew.edu.

Management of CVS episodes includes early initiation of antiemetic agents, usually beginning with intravenous ondansetron, rehydration if necessary, and facilitation of sleep. If esophageal pain and bleeding occur, gastric acid secretion should be suppressed with ranitidine. Some patients have premonitory symptoms of CVS, such as slight abdominal pain or a feeling of severe fatigue. They should attempt to abort episodes with pharmacologic or psychologic methods. Several clinical reports on the use of prophylactic drugs indicate mixed or unpredictable results. Both children and families need psychologic support. At the present time, the CVSA provides a great deal of such support, as well as education for both families and the medical profession.

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REFERENCES

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CVS exemplifies the need for precise clinical acumen in both diagnosis and treatment. Specific disorders of gastrointestinal, neurological, urological and metabolic function might not be apparent during an initial evaluation. The diagnostic challenge is heightened by the frequent development of psychologic symptoms and family disruption often seen in children with recurrent episodes of painful emesis. The case of Denise reminds us that the diagnostic evaluation is not complete until established medical causes of CVS have been investigated. That Denise seemed to be well adjusted in school and at home despite her episodes of recurrent vomiting might have been the clue to her underlying metabolic defect. An affective disorder or significant family conflict did not appear to be associated with her symptoms.

Dr. Olness noted that our inability to find a cause for CVS reflects an inadequacy in medical diagnosis rather than a psychologic diagnosis. (Could this point of view be influenced, in part, by our current knowledge that peptic ulcer disease is often caused by an infectious agent, Helicobacter pylori?) The discovery of anatomic neurological diseases, urologic disorders, and many gastrointestinal disorders should not be difficult. However, inborn errors in metabolism1 and some disorders of gastrointestinal motility might be more difficult to investigate and diagnose. The case of Denise makes it clear that the skills of selected specialists can be helpful in arriving at a treatable cause.

A fascinating hypothesis links CVS with abdominal migraine.2 A family history for migraine headaches is frequent in children with CVS. The cyclic pattern of illness with a state of well-being between episodes is similar in the two entities. Quantitative electroencephalographic changes in CVS are consis-
tent with patterns recorded in patients with migra
ne. Intravenous ondansetron, a 5-hydroxytrypt
amine-3 antagonist, is used for children with CVS,
as noted by Dr. Katz. A preliminary observation
suggests that sumatriptan, a 5-hydroxytryptamine-1
agonist, might be effective when used at the first sign
of a CVS episode.

Recurrent vomiting is a dramatic example of many
clinical situations in children and adolescents in
which the evaluation process must incorporate med-
ical and psychosocial data collection simultaneously.
When the clinician is sensitive to the primary and
secondary sources of behavioral symptoms and fam-
ily conflicts, diagnostic precision is strengthened.

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### Cyclic Vomiting

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