Abdominal Migraine and Cyclical Vomiting

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Vomiting and abdominal pain are symptoms that may arise from a number of different causes. Cyclical vomiting and abdominal migraine are terms that have been applied to a presentation characterized by its episodic pattern and intervals of complete health. The 2 share many clinical features, but it is important to distinguish them as they have different responses to therapies such as prophylactic antimigraine medications. Both are noted for the absence of pathognomonic clinical features but also for the large number of other conditions to be considered in their differential diagnoses. Definitive diagnosis is frequently delayed. It is important to carefully evaluate these patients as well-being between vomiting episodes does not guarantee the absence of organic disease. While there is a role for a basic set of diagnostic tests, there is evidence to suggest that a trial of empiric therapy with upper gastrointestinal and small-bowel radiological studies is cost-effective.

CYCLIC VOMITING SYNDROME and abdominal migraine are relatively unusual conditions that present with recurrent and severe paroxysmal vomiting or abdominal pain separated by periods of weeks or months of good health. Although first identified by Samuel Gee in 1882,[1] there was relatively little published in this area until the last 15 years. The inexperience of medical practitioners with these conditions, the absence of specific diagnostic features, and the presence of a large differential diagnosis tend to delay definitive diagnosis.

CYCLIC VOMITING

Cyclic vomiting syndrome is characterized by recurrent, stereotypical episodes of intense nausea and vomiting lasting hours to days, which are separated by symptom-free intervals. The first episodes typically begin between the ages of 2 and 9 years,[2] although it has been reported to present in early infancy and in adult life (Table 1).

The average frequency of episodes is about 12 per year, but attacks may be either regular or sporadic[3] and range from 1 to 70 per year. In most patients, the durations and symptoms experienced during episodes tend to be similar over months or years,[4] but about 15% have attacks of variable length and type.

Many families (84%)[5] are able to recognize precipitants of attacks, which may be multiple. These include stress-inducing events (47%) such as school dances, vacations, and examinations, as well as infections (44%),[6] with the attack commencing once the event was over. Other recognized precipitants include foods (28%), exercise (19%), and trauma (16%).[6]

Episodes are usually preceded by a *prodrome* of nausea, pallor, and abdominal pain that may last from a few minutes to several hours. Changes in behavior have also been noted to occur in the prodromal phase. These include withdrawal, lethargy, sleep change, and crying.[6]

Vomiting typically begins during the night or early morning.[4] It peaks in the first hour and is particularly severe, occurring up to 13 times an hour,[7] and is accompanied by retching. The emesis is often projectile (50%), containing bile (76%), mucous (72%), or blood (32%).[8] Severe nausea occurs in 76%[9] and is usually the most distressing symptom. It is unrelenting and completely unrelieved by vomiting, disappearing only when the episode is over. Many of the behavioral disturbances that can be observed are designed to lessen the nausea[10] (eg, fetal positioning, social withdrawal, compulsive drinking, turning off lights). Patients are often unwilling to swallow saliva and prefer to spit it out. Abdominal pain, which may be periumbilical or epigastric, is present in 80% of patients[9] and may be severe enough to mimic an acute abdomen. About 30% of patients have loose stools near the onset of the cyclic vomiting episodes.[4] Headaches as well as fever have been reported in about 25% of cases. Hypertension, tachycardia, and a transient leucocytosis have also been identified.[11] Dehydration and electrolyte imbalance may be severe during the vomiting phase, with about 60% requiring intravenous rehydration,[12] and others developing hematemesis from either peptic esophagitis or a Mallory-Weiss tear.

The episodes last on average 1 to 2 days, though may be longer and cease when the nausea and vomiting stop. The *recovery* phase that follows is usually fairly rapid, and is followed by a *symptom-free interval* before the next episode.

Episodes tend to recur over many years. In most cases they cease during early adolescence, but persistence through to adult life is well recognized.[2,6] Estimates of the prevalence of cyclic vomiting syndrome in childhood range from 1.9% to 2.3%.[13,14]

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Table 1. Criteria for the Diagnosis of Cyclic Vomiting Syndrome[32]

Essential criteria
Recurrent, severe, discrete episodes of vomiting
Varying intervals of normal health between episodes
Duration of vomiting episodes from hours to days
No apparent cause of vomiting with negative laboratory, radiographic. and endoscopic test results
Supportive criteria
Stereotypic pattern of vomiting, with each individual having a similar time of onset, intensity, duration, frequency, and associated symptoms
Vomiting is self-limited and resolves spontaneously if left untreated
Associated symptoms include nausea, abdominal pain, headache, motion sickness, photophobia, and lethargy
Associated signs include fever, pallor, diarrhea, dehydration, excess salivation, and social withdrawal

The cause of cyclic vomiting syndrome is still unclear. Recent hypotheses have focused on the role of autonomic instability[15] as a primary pathogenic factor. Other etiologies that have been proposed include disturbances in the hypothalamic-pituitary-adrenal axis,[16] a mitochondrial disorder,[17] and an abnormality in ion channels.[18]

MANAGEMENT OF CYCLIC VOMITING SYNDROME

In the absence of therapies that will cure cyclic vomiting syndrome, management should be directed toward establishing the diagnosis, the relief of nausea and vomiting, treatment of its acute complications, and prophylaxis.

An individualized treatment plan should be developed for each family that minimizes frustrating waiting periods in emergency rooms and hospitalizations, and also educates staff unfamiliar with the disorder. This involves developing strategies for avoidance of trigger factors, prophylactic pharmacotherapy, abortive therapy, supportive care during acute episodes, and family support.[8] There is evidence that a single diagnostic consultation with a knowledgeable clinician with whom the family establishes a good rapport will result in a significant decrease in the frequency and severity of attacks.[2,19]

There is an opportunity to abort the nausea and vomiting once it has begun. A constant intravenous infusion of the 5-HT_3 antagonist ondansetron has shown an efficacy of about 60% if given early in the attack.[8,19] If nausea persists, the benzodiazepine lorazepam has been effective as a sole antiemetic in some patients with cyclic vomiting[19] or in combination with ondansetron. Lorazepam has sedative and anxiolytic properties. Phenothiazines and metoclopramide appear to be less effective and entail the risk of inducing extrapyramidal reactions.[19] Antimigraine drugs such as sumatriptan, a 5-HT_{10} agonist, have been found to be effective in 50% of patients with cyclic vomiting syndrome.[8] It is important to place the child in a quiet environment. Failure to respond to abortive therapy is not uncommon, but should raise the possibility of a secondary pathology, such as bowel obstruction.

Once vomiting is well established, intravenous fluids are likely to be required. The glucose content may limit the degree of ketosis. Potassium supplementation will also be needed. Inappropriate secretion of antidiuretic hormone has been noted in cyclic vomiting syndrome. Intravenous fluid input should be limited if hyponatremia and low serum osmolality develop.

Periumbilical or epigastric pain may be a major feature. Nonsteroidal antiinflammatory drugs such as ibuprofen have been used to provide relief.[19] An intravenous proton pump inhibitor such as omeprazole will reduce the severity of gastritis and esophagitis.

Hypertension and tachycardia rarely require specific treatment, but should be monitored as potentially encephalopathic hypertension has been reported. Behavioral disturbances are common and may be superficially mistaken for a psychotic state.[20]

If it is not possible to bring the episode to an end pharmacologically, then an alternative option is to sedate the patient until the episode resolves spontaneously. A combination of diphenhydramine and chlorpromazine has been used effectively to induce sleep.[8,19]

Prophylactic therapy has been used in patients who have frequent, long-lasting, or difficult-to-abort episodes.[21] Amitryptyline has been shown to prevent recurrences for at least 5 months in 73% of 22 patients.[22] Cyprohepatidine provided complete protection in 4 of 6 patients over a similar period.[22] Propranolol appears to provide similar efficacy[8,21] as does erythromycin.[23] Other therapies have included homeopathic and vitamin supplements[21] as well as L-camitine.[24] No single agent is completely effective. Many of these agents also provide effective prophylaxis for migraine headaches and they appear to be most effective in children where migraine is associated with the cyclic vomiting.[12] Li et al[12] found that antimigraine prophylaxis produced at least a 50% reduction in the number of episodes in 86 children with migraine-associated cyclic vomiting syndrome but only a 36% reduction in 11 where there was no associated migraine. It is possible that these children might be better labeled as having abdominal migraine.

ABDOMINAL MIGRAINE

Abdominal migraine is characterized by recurrent, acute-onset, incapacitating, noncolicky midline abdominal pain lasting for hours and accompanied by pallor and anorexia. Vomiting may be an accompanying feature, but is often less severe.[12] There is usually a history of migraine headache either in the child or the family, but headache may be minimal or absent during the attacks.

Episodes of abdominal pain are paroxysmal and separated by symptom-free intervals of weeks to months. The labels "cyclic vomiting syndrome" and abdominal migraine" have on occasions been used interchangeably,[25] but there are significant differences between migraine-associated cyclic vomiting and non-migraine–associated cyclic vomiting that support their separation.[12] The key difference between the 2 is in the history of migraine headache. Some of the other criteria of abdominal migraine are similar to those of cyclic vomiting syndrome (Table 2). When both migraine headaches and cyclic vomiting occur in the same patient, the predominant symptom should be used as the primary label.[25]

In data obtained from a population-based study,[26] abdominal pain in children with abdominal migraine was usually described as "just sore" or "dull" (60%), but could be colicky (22%). It was periumbilical in most (78%) but could be felt diffusely in 16%.[26] The pain interfered with normal daily activities in 72%. The pain was occasionally preceded by nonspecific prodromal symptoms, such as behavior or mood changes or anorexia (14%).

Patients with abdominal migraine tend to experience more social withdrawal and photophobia with episodes, and are more likely to have triggering events such as psychological stress, physical exhaustion, and motion sickness than patients with cyclic vomiting syndrome.[12] In the past these features have contributed to the view that this condition is psychogenic.[27] Although there is controversy surrounding the relationship between the diagnosis of abdominal migraine and that of migraine which fulfills the diagnostic criteria of the International Headache Society,[26,28] the similarities between the 2 in terms of demographic features, associated recurrent conditions, precipitating trigger factors, associated symptoms during attacks, and relieving factors are so close as to suggest that they share a common pathogenesis.[26]

Table 2. Criteria for the Diagnosis of Abdominal Migraine[3]

In the preceding 12 months, 3 or more paroxysmal episodes of intense, acute midline abdominal pain lasting 2 hours to several days, with intervening symptom-free intervals lasting weeks to months; and
Evidence of metabolic, gastrointestinal, and central nervous system structural or biochemical disease is absent; and
Two or more of the following features:
Headache during episodes
Photophobia during episodes
Family history of migraine
Headache confined to 1 side only
An aura or warning period consisting of visual disturbances (eg, blurred or restricted vision), sensory symptoms (eg, numbness or tingling), or motor abnormalities (eg, slurred speech, inability to speak, paralysis).

Table 3. Abbreviated Differential Diagnosis of Cyclic Vomiting[2]

Gastrointestinal
Pancreatitis
Intermittent small-bowel obstruction
Chronic idiopathic intestinal pseudo-obstruction
Crohn's disease
Neurological
Brain tumor with raised intracranial pressure
Brain stem tumor
Subdural hemotoma
Familial dysautonomia
Urinary
Obstructive uropathy
Endocrine
Adrenal insufficiency
Metabolic
Ornithine transcarbamylase deficiency
Methylmalonic acidemia
Acute intermittent porphyria

The mean age of onset of abdominal migraine is reported to be 7 years[26] and the estimates of the prevalence in childhood range from 2.4% to 4.1%,[26,29] In a 10-year follow-up study of 54 children with abdominal migraine, abdominal symptoms had resolved in 61%, but 70% had developed typical migraine headaches.[27]

Management of Abdominal Migraine

As with cyclic vomiting syndrome, the first priority should be toward firmly establishing the diagnosis. Many families are content with this and reassurance that the episodes are not the result of a serious pathology. Headaches are not necessarily a feature at first presentation, but this should not prevent a trial of a migraine therapy. If vomiting predominates, the child should be treated as for cyclic vomiting. There is little evidence on which to base recommendations for drug therapy of abdominal migraine. It has been suggested that nasal sumatriptan may be effective in treating acute episodes of abdominal pain.[28] Pizotifen, propranolol, and cyproheptatidine[28] have been shown to be effective prophylactics.

DIFFERENTIATION OF CYCLIC VOMITING AND ABDOMINAL MIGRAINE FROM OTHER DISORDERS

Abdominal pain and vomiting have a wide differential diagnosis in childhood (Table 3). Unfortunately, both cyclic vomiting and abdominal migraine are relatively unusual conditions and lack specific diagnostic features. It has been estimated that approximately 12% of patients with clinical features apparently suggestive of cyclic vomiting syndrome actually have specific and potentially serious gastrointestinal, renal, neurologic, or metabolic diseases.[2,7,30,31] No estimate has been published for abdominal migraine, but it is likely that the proportion may be much greater.

An initial evaluation should include a careful history that may elucidate previous episodes, which are often stereotyped. A prodromal phase may be able to be identified. A history of migraine-type headaches may be present in either the child or a close family member. Physical examination of the child with cyclic vomiting syndrome or abdominal migraine during the symptom-free period is entirely unremarkable. The most important systems to examine in order to exclude other differentials include the gastrointestinal tract and the central nervous and urinary systems. Normal growth is usually used as a parameter to exclude "nonorganic" disease, but there is no published information on growth patterns in children with cyclic vomiting syndrome or abdominal migraine.

The wide differential diagnosis of abdominal pain and vomiting in children has led to the development of long lists of recommended diagnostic studies to confirm the diagnosis in suspected cyclic vomiting syndrome or abdominal migraine.[2] Using decision analysis software, Olson and Li[30] carried out a comparison of the cost-effectiveness of:

1. extensive diagnostic evaluation,
2. empiric treatment alone, and
3. upper gastrointestinal radiology with small-bowel follow-through plus empiric treatment.

The prophylactic drugs that were included in the model were propranolol, cyproheptadine, and amitryptiline. The extensive diagnostic evaluation group included an upper and small-bowel series together with esophago gastroduodenoscopy, sinus films, head computerized tomography or magnetic resonance imaging, abdominal ultrasound, metabolic testing during the episode (serum glucose, electrolytes, ammonia, lactate, camitine, complete blood count, sedimentation rate, alanine aminotransferase, γ-glutamyl transferase, amylase, lipase, urinalysis, urinary organic acids, δ-aminolevulinic acid, porphobilinogen). On the basis of this study, upper gastrointestinal radiology with small-bowel follow-though plus empiric antimigraine treatment for an initial period of 2 months was the most cost-effective strategy. The cost of complications of a missed malrotation with volvulus was higher than that of adding the radiological studies to each evaluation. This study did not, however, factor in the costs associated with possible litigation that increasingly encourages "defensive" laboratory investigations.

Table 4. Initial Diagnostic Studies That Should Be Considered in Children Presenting with Possible Cyclic Vomiting Syndrome or Abdominal Migraine

Blood studies
Hemoglobin, white count, and differential
C-reactive protein
Electrolytes, creatinine, and glucose
Liver function tests
Pancreatic enzymes
Pregnancy test
Urine and stool studies
Urinalysis with microscopy and culture
Stool occult blood and microscopy
Radiological studies
Ultrasound of liver, biliary tract, pancreas, and kidneys
Contrast study of upper gastrointestinal tract and small bowel
Magnetic resonance imaging of brain
Endoscopy
Esophagogastroduodenoscopy
Colonoscopy with ileoscopy (to exclude Crohn's)

Other authors have suggested that stool should be obtained for occult blood and microscopy, as well as a pregnancy test and blood lead[4] (Table 4).

CONCLUSION

In the absence of pathognomonic features, cyclic vomiting syndrome and abdominal migraine are often diagnosed through a process of exclusion. It is clear that the most important evaluation of a child who presents with recurrent paroxysmal vomiting or abdominal pain is a careful history and physical examination. Laboratory investigations, endoscopy, and imaging should be requested to answer questions raised during this initial evaluation. If there is a strong clinical suspicion and no evidence of another significant pathological process, there is a good case to be made for an empirical trial of an antimigraine therapy.

REFERENCES

1. Gee S: On fitful or recurrent vomiting. St Bartholomew's Hosp Rep 18:1-6, 1882

2. Fleisher DR: Cyclic vomiting, in Hyman PE, Di Lorenzo C (eds): Pediatric Gastrointestinal Motility Disorders New York, Academy Professional Information Services, Inc, 1994, pp 89-103

3. Rasquin-Weber A, Hyman PE, Cucchiara S, et al: Childhood functional gastrointestinal disorders. Gut 45:1160-1168, 1999 (suppl 2)

4. Fleisher DR, Matar M: The cyclic vomiting syndrome: a report of 71 cases and literature review. J Pediatr Gastroenterol Nutr 17:361-369, 1993

5. Forbes D, Withers G, Silburn S, McKelvey R: Psychological and social characteristics and precipitants of vomiting in children with cyclic vomiting syndrome. Digest Dis Sci 44:19S-22S, 1999

6. Withers GD, Silburn SR, Forbes DA: Precipitants and aetiology of cyclic vomiting syndrome. Acta Paediatr 87:272-277, 1998

7. Pfau BT, Li BU, Murray RD, Heitlinger LA, McClung HJ, Hayes JR: Differentiating cyclic from chronic vomiting patterns in children: quantitative criteria and diagnostic implications. Pediatrics 97:364-368, 1996

8. Sundaram S, Li BU: Cyclic vomiting syndrome. eMedicine.com. www.emedicine.com/ped/topic 2910.htm updated August 10, 2002; accessed April 26, 2003

9. Li BU, Fleisher DR: Cyclic vomiting syndrome: features to be

explained by a pathophysiologic model. Digest Dis Sci 44:13S-18S, 1999

10. Li BU, Balint JP: Cyclic vomiting syndrome: evolution in our understanding of a brain-gut disorder. Adv Pediatr 47:117-160, 2000

11. Millichap J, Lombroso C, Lennox W: Cyclic vomiting as a form of epilepsy in children. Pediatrics 15:705-714, 1955

12. Li BU, Murray RD, Heitlinger LA, Robbins JL, Hayes JR: Is cyclic vomiting syndrome related to migraine? J Pediatr 134:567-572, 1999

13. Abu-Arafeh I, Russell G: Cyclical vomiting syndrome in children: a population-based study. Pediatr Gastroenterol Nutr 21:454-458, 1995

14. Cullen KJ, MacDonald WB: The periodic syndrome: its nature and prevalence. Med J Australia 2:167-173, 1963

15. To J, Issenman RM, Kamath MV: Evaluation of neurocardiac signals in pediatric patients with cyclic vomiting syndrome through power spectral analysis of heart rate variability. J Pediatr 135:363-366, 1999

16. Tache Y: Cyclic vomiting syndrome: the corticotropin-releasing-factor hypothesis. Digest Dis Sci 44:79S-86S, 1999

17. Boles RG, Williams JC: Mitochondrial disease and cyclic vomiting syndrome. Digest Dis Sci 44:103S-107S, 1999

18. Ptacek LJ: Channelopathies: ion channel disorders of muscle as a paradigm for paroxysmal disorders of the nervous system. Digest Dis Sci 44:94S-96S, 1999

19. Fleisher DR: Management of cyclic vomiting syndrome. J Pediatr Gastroenterol Nutr 21Suppl 1:S52-S56, 1955

20. Sato T, Igarashi N, Minami S, et al: Recurrent attacks of vomiting, hypertension and psychotic depression: a syndrome of periodic catecholamine and prostaglandin discharge. Acta Endocrinol 117:189-197, 1988

21. Forbes D, Withers G: Prophylactic therapy in cyclic vomiting syndrome. J Pediatr Gastroenterol Nutr 21Suppl 1:S57-S59, 1995

22. Andersen JM, Sugerman KS, Lockhart JR, Weinberg WA: Effective prophylactic therapy for cyclic vomiting syndrome in children using amitriptyline or cyproheptadine. Pediatrics 100:977-981, 1977

23. Vanderhoof JA, Young R, Kaufman SS, Emst L: Treatment of cyclic vomiting in childhood with erythromycin. J Pediat Gastroenterol Nut 17:387-391, 1993

24. Van Calcar SC, Harding CO, Wolff JA: L-carnitine administration reduces number of episodes in cyclic vomiting syndrome. Clin Pediatr 41:171-174, 2002

25. Symon DN: Is cyclical vomiting an abdominal form of migraine in children? Digest Dis Sci 44:23S-25S, 1999

26. Abu-Arafeh I, Russell G: Prevalence and clinical features of abdominal migraine compared with those of migraine headache. Arch Dis Childh 72:413-417, 1995

27. Dignan F, Abu-Arafeh I, Russell G: The prognosis of childhood abdominal migraine. Arch Dis Childh 84:415-418, 2001

28. Russell G, Abu-Arafeh I, Symon DN: Abdominal migraine: evidence for existence and treatment options. Paediatr Drugs 4:1-8, 2002

29. Mortimer MJ, Kay J, Jaron A: Clinical epidemiology of childhood abdominal migraine in an urban general practice. Dev Med Child Neurol 35:243-248, 1993

30. Olson AD, Li BU: The diagnostic evaluation of children with cyclic vomiting: a cost-effectiveness assessment. J Pediatr 141:724-728, 2002

31. Li BU, Murray RD, Heitlinger LA, Robbins JL, Hayes JR: Heterogeneity of diagnoses presenting as cyclic vomiting. Pediatrics 102:583-587, 1998

32. Consensus criteria from the International Symposium on Cyclical Vomiting Syndrome. J Pediat Gastroenterol Nutr 21:6, 1995