



Rare disorders can be an underlying cause of cyclic vomiting: Familial Mediterranean fever, *Helicobacter pylori* gastritis, and cavernous transformation of the portal vein

STOMACH

Ödül Egritaş Gürkan, Aysel Ünlüsoy Aksu, Zeliha Demirtaş, Buket Dalgıç

Department of Pediatric Gastroenterology, Gazi University Faculty of Medicine, Ankara, Turkey

ABSTRACT

Background/Aims: Considering the etiology of cyclic vomiting syndrome (CVS) in childhood, a variety of underlying organic causes has been clearly identified in the literature. The aim of this study was to emphasize that endoscopic evaluation in the first step may help diagnosis and treatment in patients with CVS, unlike the CVS-related "North American Society for Pediatric Gastroenterology, Hepatology and Nutrition" (NASPGHAN) consensus statement in 2008.

Materials and Methods: The medical files of patients with vomiting complaints admitted to our tertiary center between the years 2007 and 2012 were analyzed retrospectively. Patients were identified according to the International Classification of Diseases (ICD) codes at their initial presentation, including vomiting.

Results: A total of 815 patients with vomiting complaints were evaluated. Of the 379 patients who presented with vomiting only, 336 patients were already being followed for chronic vomiting. Cyclic vomiting was detected in 31 out of 336 patients.

Conclusion: In our series, familial Mediterranean fever (FMF), cavernous transformation of the portal vein, and *Helicobacter pylori* (HP) gastritis presented with CVS for the first time in the pediatric age group. We emphasize that endoscopic evaluation in patients with CVS should be performed as the first step for appropriate diagnosis and treatment.

Keywords: Cyclic vomiting, familial Mediterranean fever, gastritis, cavernous transformation, children

INTRODUCTION

Cyclic vomiting is a chronic disease with relapsing vomiting attacks. The first pediatric descriptions of cyclic vomiting syndrome (CVS) were provided in the French literature by Heberden in 1806 and in the English literature by Gee in 1882 (1-3). CVS may be easily diagnosed from medical history; however, it is a complex disease for which physicians have to perform a variety of tests to illustrate accompanying organic pathology. Many diseases such as brain tumors, intestinal obstruction, pancreatitis, obstructive uropathy, metabolic disorders, and familial dysautonomia may mimic CVS. Tests to be performed to identify an underlying etiology in CVS are clearly indicated in the "North American Society for Pediatric Gastroenterology, Hepatology and Nutrition" (NASPGHAN) consensus statement in 2008 (4). According to the consensus statement, diagnostic endoscopic evaluation is necessary in patients with CVS in the presence of warning symptoms. Unlike the NASPGHAN

consensus statement in 2008, according to our study results, we believe that performing endoscopic evaluation as the first step may help in the diagnosis and treatment, even in the absence of warning symptoms. Also, we emphasized the presence of cyclic vomiting association with familial Mediterranean fever (FMF), cavernous transformation of the portal vein, and *Helicobacter pylori* (HP) gastritis for the first time in a pediatric age group in the literature.

MATERIALS AND METHODS

The medical files of patients with vomiting complaints admitted to our tertiary center between the years 2007 and 2012 were analyzed retrospectively. Patients were identified according to the International Classification of Diseases (ICD) codes at their initial presentation. Patients were derived from the hospital information system with the following diagnosis and ICD codes: nausea and vomiting, R11; vomiting associated with other

Address for Correspondence: Ödül Egritaş Gürkan, E-mail: odulmd2003@yahoo.com

Received: March 30, 2015

Accepted: August 23, 2015

Available Online Date: October 26, 2015

© Copyright 2015 by The Turkish Society of Gastroenterology • Available online at www.turkjgastroenterol.org • DOI: 10.5152/tjg.2015.0015

psychological disturbances, F50.5; Vomiting following gastrointestinal surgery, K91.0; and vomiting in newborn, P92.0; Patients having other ICD codes in addition to the reference codes were excluded.

If the vomiting complaint lasts for more than a month, it was defined as chronic vomiting. To elucidate the etiology of chronic vomiting, the following analyses were performed for the patients according to their age, medical history, and physical examinations with changing priorities: urine analysis, urine culture, complete blood count (CBC), liver enzymes, kidney function tests, serum electrolytes, creatinine phosphokinase, arterial blood gases, amylase, lipase, thyroid function tests, erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), and metabolic tests (urine blood amino acids, urine organic acids, tandem mass, reductant substance in urine, ammonia, lactic acid/pyruvic acid), total IgA, Celiac serology, abdominal ultrasound/computed tomography (CT), upper gastrointestinal series, endoscopy, electroencephalography (EEG), cranial magnetic resonance imaging (MRI) examinations, and FMF mutation analysis.

Metabolic tests and cranial imaging are indicated to all patients in presence of papilledema, motor and mental retardation and abnormal eye movements. In our series, fundus examinations were performed for all patients by a neurologist or ophthalmologist regardless of the age and motor and mental development for the presence of papilledema. During follow-up, metabolic tests were performed for conditions such as papilledema, neuromotor retardation, or uncontrolled cyclic vomiting after treatment. Thus, metabolic tests were repeated twice in such patients, including attack periods.

The diagnosis of CVS is made using the diagnostic criteria in 2008. Diagnostic criteria should include all of the following parameters: a) stereotypical episodes of vomiting regarding onset (acute) and duration (less than 1 week), b) three or more discrete episodes in the prior year, and c) absence of nausea and vomiting between episodes (4).

The files of patients diagnosed with CVS were examined retrospectively in detail. How many admittance were needed till the diagnosis, number of hospitalizations, social and economical status, presence of a loss prior to the start of attacks, presence of a documented failure in patient's life, and decrease in the quality of life during vomiting attacks in out of hospital period (such as missing school, unable to watch television, unable to play games, continuous stay in bed) were noted from the files. Families of the patients who did not attend follow-up appointments were contacted by telephone calls. Patients who did not attend follow-up appointments were questioned for the following parameters: where and how do they continue their follow-ups, drug usage details, when the complaints subsided, additional complaints or diseases, and finally, continuance of follow-ups.

RESULTS

A total of 815 patients with vomiting complaints were admitted to our clinic between the years 2007 and 2012. Patients having additional ICD codes other than vomiting-related reference codes were excluded. Thus, a total of 379 patients were enrolled in the study, and patient files were analyzed retrospectively. In this group, there were 336 patients identified with CVS. The study flow chart of patients admitted with vomiting complaints is listed in Figure 1.

In the follow-up of the patients with CVS, the final diagnoses of the patients were as follows: gastroesophageal reflux (288 patients), erosive gastritis (2 patients), rotation anomaly (3 patients), eosinophilic esophagitis (3 patients), gluten allergy (1 patient), Celiac disease (1 patient), superior mesenteric artery syndrome (SMA) (1 patient), pyloric stenosis (1 patient), antral web (1 patient), paraduodenal pancreatic cysts (1 patient), intracranial mass (2 patients), and FMF disease with upper gastrointestinal involvement with esophagitis and gastritis (1 patient). There were 31 patients with CVS diagnosis.

The demographic characteristics, etiologies, and follow-ups of 31 patients diagnosed with CVS are shown in Table 1.

In 6 of the 31 patients diagnosed with CVS, an underlying organic disease association was found during the follow-up period. Regarding the etiology of these 6 patients, the diagnoses were as follows: HP gastritis (3 patients), FMF (1 patient), portal hypertension (cavernous transformation of the portal vein) (1 patient), and duplication cyst (1 patient). The remaining 25 patients were diagnosed with idiopathic CVS.

The clinical and laboratory characteristics of the 6 patients who presented with CVS are given in Tables 2,3.

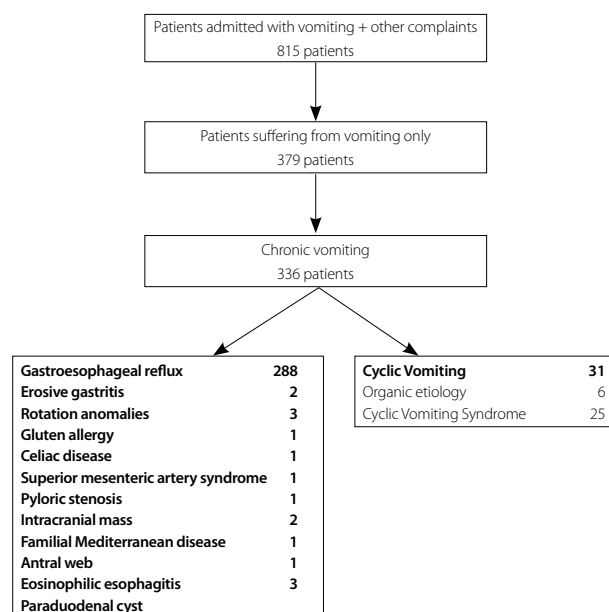


Figure 1. Study flow chart of patients with vomiting complaints

Table 1. Demographic characteristics, etiologies, and follow-ups of 31 patients diagnosed with cyclic vomiting syndrome

Patients diagnosed with cyclic vomiting syndrome	n=31
Gender	Female 14 (45.2%) Male 17 (54.8%)
Age at diagnosis (months)	Median: 84 (SD±56.84) (min: 18–max: 204)
Start of complaints (months)	Median: 48 (SD±46.62) (min: 6–max: 156)
Delay time until the diagnosis (months)	Median: 24 (SD±32.53) (min: 4–max: 132)
Vomiting frequency (during an attack)	
<10 times/day	15 (48.4%)
>10 time/day	10 (32.3%)
Too many to count	6 (19.4%)
Attack duration (days)	Median: 2 (SD±2.56) (min: 1–max: 10)
Attack interval (days)	Median: 30 (SD±41.79) (min: 4–max: 110)
Family history for migraine	12 (38.7%)
Presence of migraine	1 (3.2%)
Family history for headache	14 (45.2%)
Presence of headache	3 (9.7%)
Aura period before attacks	9 (29%)
Follow-up period of patients (months)	Median: 4 (SD±17.19) (Min: 1–max: 67)

Table 2. Demographic characteristics of the patients presented with cyclic vomiting syndrome

Diagnoses of the patients presented with cyclic vomiting syndrome	Age at diagnosis/gender	Age at onset of complaints	Body weight/Percentile (pr)	Height/Percentile (pr)	Pathologic findings in physical examination	Attack interval	Attack duration	Vomiting frequency
Patient 1 (Portal HT)	3.5 years/female	3 years	17.5 kg (10–25 pr)	116 cm (50–75 pr)	Splenomegaly 4 cm under costal arc	In every 15 days	4–5 days	<10 times/day
Patient 2 (FMF)	14 years/female	13 years	48 kg (25–50 pr)	156 cm (25–50 pr)	None	Once in every 2 months	1 day	>10 times/day
Patient 3 (HP+ gastritis)	9 years/male	7 years	24.1 kg (10–25 pr)	126 cm (10–25 pr)	Epigastric tenderness	Once in a month	10 days	<10 times/day
Patient 4 (HP+ gastritis)	7 years/female	6 years	25 kg (75–90 pr)	126 cm (90–97 pr)	None	Once in every 3 months	4 days	>10 times/day
Patient 5 (HP+ gastritis)	10 years/male	5 years	13.4 kg (10–25 pr)	96 cm (25–50 pr)	Epigastric tenderness	Once in a month	1 day	>10 times/day
Patient 6 (duplication cyst)	14 years/male	13 years	54 kg (50–75 pr)	168 cm (75–90 pr)	None	Once in a week	2 days	<10 times/day

FMF: familial Mediterranean fever; HP: *helicobacter pylori*; HT: hypertension

Statistical analysis

The Statistical Package for the Social Sciences (SPSS) v.16.0 software package for Windows (SPSS Inc., Chicago, Illinois, USA) was used for statistical analysis. Numerical data were expressed as a percentage, and measurement data were expressed as the mean±standard deviation (SD). Differences were evaluated with the χ^2 test.

Parents and patients were informed about endoscopy, colonoscopy, and enteroscopy procedures, and the related written informed consents were obtained. The local ethics committee approved this retrospective study.

DISCUSSION

The most important feature of CVS is the completely healthy state between episodes of vomiting (5). Each episode duration and recurrence interval varies according to the patient, generally in order (5). In 1995, Abu-Arafah et al. (6) reported the incidence of CVS in the pediatric age group as 2.3% in their study. In 2006, Uc et al. (7) reported an incidence of 0.8% in African-American children. In 2008, Fitzpatrick et al. (8) reported an incidence of 3.15/100.000 in Ireland. Ertekin et al. (9) from Turkey reported the presence of CVS in 1263 school children (ages ranging from 7 to 14 years) and reported the prevalence as

Table 3. Evaluation of patients presented with cyclic vomiting syndrome

Patients presented with cyclic vomiting syndrome	Endoscopy	Biopsy	Imaging	Treatment	Follow-up
Patient 1	Grade 3 esophageal varices, portal gastropathy	None	Doppler ultrasound and CT angiography: portal cavernous transformation of the portal vein	Propranolol HCl, PPI	5 years. Shunt operation in 7 years of age. Not using propranolol HCl. No complaints
Patient 2	Normal upper gastrointestinal endoscopy	Normal. No amyloid deposit	None	Colchicine	1 year. No complaints
Patient 3	Antral nodular gastritis	HP+ gastritis	None	PPI and antibiotic treatment	2 months
Patient 4	Antral nodular gastritis	HP+ gastritis	Upper gastrointestinal series: normal	PPI and antibiotic treatment	4 months
Patient 5	Pangastritis	HP+ gastritis	Upper gastrointestinal series: normal	PPI and antibiotic treatment	3 months
Patient 6	Pangastritis megabulbus	HP- gastritis	Upper gastrointestinal series: no passage detected after duodenum second portion	PPI	2 years. No complaints after gastrojejunostomy

PPI: proton pump inhibitor; CT: computed tomography; HP: *helicobacter pylori*

1.9%. Although the study method was different from our study, Hejazi et al. (10) diagnosed CVS in 17 out of 545 patients (3.1%) referred to their clinic with nausea, vomiting, and other motility disorders between 2004 and 2008. In our study, 31 out of 336 patients (9.22%), who were followed because of chronic vomiting in the last 5 years, were diagnosed with CVS. In our study, the incidence of CVS was found to be higher than other studies in the literature. This point may be related to the limited study group as chronic vomiting and also being a referral center as well.

If CVS comes to mind, it may be easily diagnosed with history. However, diagnoses such as urinary tract infections, food poisoning, gastroesophageal reflux, and psychogenic vomiting may delay diagnosis. Liao et al. (11) reported the diagnostic delay period as 2.1 ± 2.2 years in their study of 24 children with CVS. Haghighat et al. (12) from southern Iran noted the diagnostic delay period as 2 ± 1.81 years in their study of 181 patients with CVS. Similarly, Gokhale et al. (13) study showed the diagnostic delay period as 2.2 years. In our study, the median time for onset of complaints was determined as 48 months, while the median age at diagnosis was 84 months. We observed a diagnostic delay period of 3 years. We noted that the most common diagnosis in other centers before admittance to our hospital was medical treatment-resistant reflux. On the other hand, urinary tract infection or somatization diagnoses were also present other than treatment-resistant reflux. The most striking example of this phenomenon was a 16-year-old female patient whose vomiting was thought to be due to somatization and was being followed in a psychiatric ward. The frequency of her vomiting attacks was described as once a month, particularly during menstrual periods, and severe enough to visit the emergency room, lasting up to 1 week. The patient had failed to at-

tend school for over a year, and the absence of a psychogenic cause led to a gastroenterology consultation. The patient was diagnosed with CVS and received benefit from treatment after the initiation of propranolol. Currently, the patient has completed her college education.

Thorough investigations are required to distinguish CVS from various organic disorders presented with CVS. Cyclic vomiting occurs not only in CVS patients but also in other organic diseases clinically mimicking CVS. Thus, all possible organic causes of CVS have to be ruled out for the accurate diagnosis of CVS. The following diseases and disorders have to be considered for the differential diagnosis of CVS: bowel obstruction (14,15), pancreatic diseases (16,17), parasitic infestations (18), migraine (19), epilepsy (20), space-occupying central nervous system lesions (21,22), diabetes mellitus (23), Addison's disease (24), pheochromocytoma (25), aminoaciduria, organic aciduria, fatty acid oxidation disorders, mitochondrial disorders, metabolic diseases such as urea cycle defects and porphyrias (26-30), and pelvi-ureteric junction obstruction (31,32).

In our study, etiologic organic causes for CVS were observed in 6 out of 31 patients (19.3%). Elimination of the underlying pathology resulted in a decline in the cyclic vomiting state. The most important feature of these pediatric age group patients is the fact that cavernous transformations of the portal vein and FMF related to the etiology of CVS have not been highlighted in the literature. The demographic and laboratory data of patients presented with CVS and having etiologic organic causes are shown in Tables 2,3.

We evaluated the CVS patients with an organic etiology. Our first patient was a 3.5-year-old girl who was referred because

of episodes of vomiting in every 15 days in the last 6 months. The patient's medical history revealed a 6-month therapy for gastroesophageal reflux refractory to treatment in a different center. CVS diagnosis was defined after medical history. Upon detection of splenomegaly in physical examination, further tests lead to portal hypertension diagnosis, secondary to cavernous transformation of the portal vein. Esophageal varices were present in the endoscopic evaluation, and propranolol treatment was initiated for both portal hypertension and cyclic vomiting. The patient received propranolol treatment till the operation and did not encounter any vomiting attacks. Treatment was stopped after shunt operation, and the patient has no vomiting attacks at present.

Our second patient was a 14-year-old female who was followed in the pediatric nephrology department for 4 years with FMF disease diagnosis. The patient was under colchicine treatment, and had 10 or more vomiting attacks per day, generally lasting for a day, in a cycle of every 2 months for the last year. After obtaining more in-depth details of the patient's medical history, it was learned that the patient had irregular colchicine usage in the last 2 years and even discontinuation of usage in recent months. CBC, biochemistry tests, metabolic tests, endoscopy, upper gastrointestinal series, and fundus examination were performed for the exclusion of organic pathology accompanying cyclic vomiting. Physical examination and laboratory investigations revealed no pathological findings. Vomiting attacks did not occur with the regular use of colchicine in an appropriate dose during follow-up for 2.5 years. The patient was diagnosed with FMF disease who presented with CVS. The emergence of cyclic vomiting after interruption in colchicine usage and disappearance in regular usage in addition to the absence of any accompanying etiologic factors for cyclic vomiting reminded us once again that FMF disease may be present in many different forms. FMF may present itself with vomiting (33,34).

The third, fourth, and fifth patients were at ages 9, 7, and 10 years, respectively and did not have classical dyspeptic complaints such as halitosis, abdominal pain, bitter taste, and early satiety. CBC, biochemical panel, urine culture, metabolic tests, upper gastrointestinal series, and fundus examinations were performed, and no pathological findings were present. Endoscopic views of all three patients were compatible with antral nodular gastritis, and biopsies were reported as HP+ gastritis. Treatment using antibiotics and proton pump inhibitors (PPIs) was initiated, and no complaints were seen. It was observed that patients failed to comply with follow-up appointments as the complaints disappeared. Parents were contacted by telephone calls after appointment breaks for 2 years, 19 months, and 1 year respectively. The response of the parents revealed that the patients had not been followed in any other center as their complaints disappeared.

In 2011, Koletzko et al. (35) clearly defined treatment and follow-up protocols for HP infections in childhood. The HP work-

ing groups of the European Society of pediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN) and NASPGHAN states that the relationship between HP infection and diseases such as otitis media, upper respiratory tract infection, periodontal disease, food allergies, sudden infant death syndrome, idiopathic thrombocytopenic purpura, and short stature are not sufficiently demonstrated in the literature. Recommendations of the working group also states that HP testing and treatment may be considered in refractory iron deficiency anemia after the exclusion of other causes, and treatment may be proposed to HP-infected patients having first-degree relatives with a history of gastric cancer. The above guideline recommends treatment in the presence of HP+ peptic ulcer disease. HP infection as a cause for chronic vomiting is defined in the literature (36). We observed that HP infection may be presented as cyclic vomiting and the disappearance of the complaints after treatment for the first time in the pediatric age group. The presence of HP+ gastritis was shown in three patients with CVS in our study. Although the prevalence of HP+ is high in Turkey, the disappearance of complaints after HP eradication in our patients enabled us to infer that HP gastritis is the cause of cyclic vomiting. We did not need any other treatment for cyclic vomiting after successful HP eradication in the follow-up period. Despite few cases and studies, we wanted to highlight that HP+ gastritis may be presented with cyclic vomiting in childhood and needs to be treated.

Our last patient was a 14-year-old male patient who had vomiting attacks lasting for 2 days, once a week for the last 1 year. CBC, biochemical panel, urine cultures, and fundus examinations were normal. Endoscopy revealed a megabulbus appearance (Figures 2,3). Upon monitoring the megabulbus appearance during endoscopy, upper gastrointestinal series were performed for a suspected distal obstruction. Transition to the distal section of the second part of duodenum was absent. Abdominal tomography and ultrasonography confirmed the presence of obstruction; however, they failed to clarify the etiology of obstruction. The patient underwent an operation, and the postoperative diagnosis was reported as duplication cyst. No vomiting attack was observed during a 1-year postoperative follow-up.

As stated in the NASPGHAN consensus statement on the diagnosis and management of CVS in 2008 (4), blood electrolytes, glucose, blood urea nitrogen (BUN), creatinine, and radiological examination of the upper gastrointestinal system are the first step tests to be performed (29). As indicated in the consensus, in the presence of warning signs such as bilious vomiting, hematemesis, or severe abdominal tenderness, abdominal radiology and endoscopic evaluation are recommended. In our study, pathological physical examination signs were detected in only 3 out of 6 patients with an organic etiology (splenomegaly: 1 patient, epigastric tenderness: 2 patients). Although there was a lack of any pathology on physical examination and warning symptoms in the other 3 patients, pathological

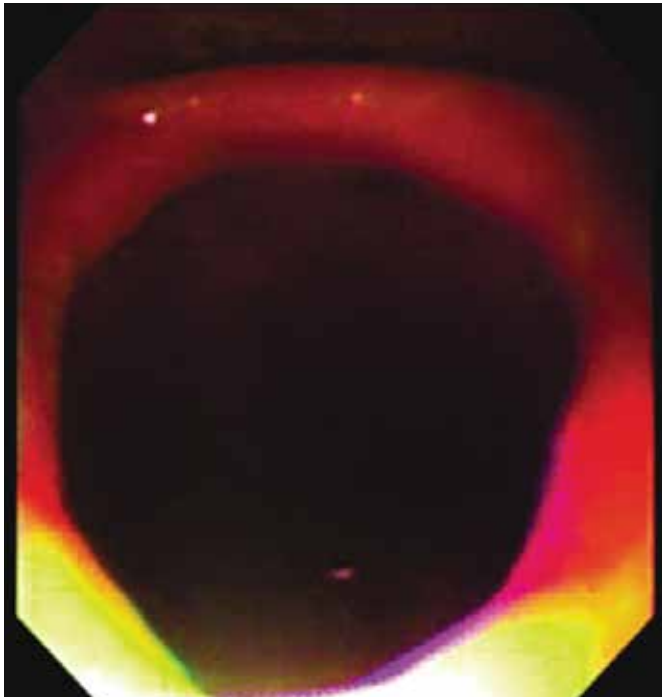


Figure 2. Enlarged pyloric ring.

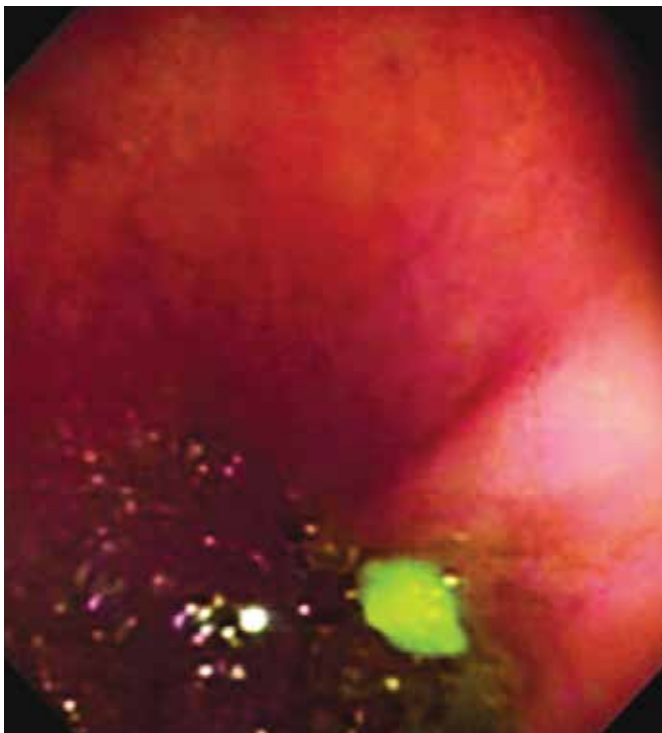


Figure 3. Megabulbus appearance in endoscopy.

signs were observed in 2 patients during endoscopy (nodular gastritis, megabulbus). Etiological factors were identified only through these pathological endoscopic appearances. To evaluate the results of our study, CBC, biochemical panel, and upper gastrointestinal series were performed for all patients as the first step. However, in our study, additional endoscopic evaluations were performed for all patients, unlike the 2008 NASPGHAN consensus statement. Based on our own study, we

believe that performing endoscopic evaluation as the first step may help in the diagnosis and treatment, even in the absence of warning symptoms.

As a result, CVS may be easily diagnosed from a patient's medical history; however, it may be defined as a complex disease. Physicians may be forced to perform a variety of tests to identify an accompanying organic pathology and attempt to administer various medications during follow-up. After reviewing the literature, we learned that many diseases may manifest themselves as CVS in the pediatric age group. In our series, apart from the literature, we observed that FMF disease, cavernous transformation of the portal vein, and HP gastritis presented with CVS for the first time in the pediatric age group. HP gastritis may manifest itself as cyclic vomiting, and even without additional dyspeptic complaints, treatment of HP may be useful. Contrary to the NASPGHAN consensus statement, endoscopic evaluation may be performed in the first step even without the presence of warning symptoms. In our study, three patients without warning symptoms were diagnosed through endoscopic findings. To the best of our knowledge, based on the studies and presented case reports in the literature, demonstrating underlying etiology and determining the appropriate treatment for the patient is more challenging than diagnosing the disease.

Ethics Committee Approval: Ethics committee approval was received for this study.

Informed Consent: Written informed consent was obtained from patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - Ö.E.G.; Design - Ö.E.G.; Supervision - Ö.E.G., A.U.A.; Resource - Ö.E.G., A.U.A., Z.D.; Materials - Ö.E.G., A.U.A.; Data Collection and/or Processing - Ö.E.G., A.U.A.; Analysis and/or Interpretation - Ö.E.G.; Literature Search - Ö.E.G.; Writing - Ö.E.G.; Critical Reviews - Ö.E.G., B.D.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

REFERENCES

1. Heberden W. Commentaries on the History and Causes of Diseases, 3rd edn. London: Payne & Foss; 1806.
2. Gee S. On fitful or recurrent vomiting. St Bartholomews Hosp Rep 1882; 18: 1-6.
3. Ravelli AM. Cyclic vomiting syndrome. J Pediatr Gastroenterol Nutr 2001; 32 Suppl 1: S14-5. [\[CrossRef\]](#)
4. Li BU, Lefevre F, Chelimsky GG, et al. North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition consensus statement on the diagnosis and management of cyclic vomiting syndrome. J Pediatr Gastroenterol Nutr 2008; 47: 379-93. [\[CrossRef\]](#)
5. Li BU. Cyclic vomiting syndrome: a pediatric Rorschach test. J Pediatr Gastroenterol Nutr 1993; 17: 351-3. [\[CrossRef\]](#)
6. Abu-Arafeh I, Russell G. Cyclical vomiting syndrome in children: a population-based study. J Pediatr Gastroenterol Nutr 1995; 21: 454-8. [\[CrossRef\]](#)

7. Uc A, Hyman PE, Walker LS. Functional gastrointestinal disorders in African American children in primary care. *J Pediatr Gastroenterol Nutr* 2006; 42: 270-4. [\[CrossRef\]](#)
8. Fitzpatrick E, Bourke B, Drumm B, Rowland M. The incidence of cyclic vomiting syndrome in children: population-based study. *Am J Gastroenterol* 2008; 103: 991-5. [\[CrossRef\]](#)
9. Ertekin V, Selimoğlu MA, Altnkaynak S. Prevalence of cyclic vomiting syndrome in a sample of Turkish school children in an urban area. *J Clin Gastroenterol* 2006; 40: 896-8. [\[CrossRef\]](#)
10. Hejazi RA, Patil H, McCallum RW. Dumping syndrome: establishing criteria for diagnosis and identifying new etiologies. *Dig Dis Sci* 2010; 55: 117-23. [\[CrossRef\]](#)
11. Liao KY, Chang FY, Wu LT, Wu TC. Cyclic vomiting syndrome in Taiwanese children. *J Formos Med Assoc* 2011; 110: 14-8. [\[CrossRef\]](#)
12. Haghighat M, Rafie SM, Dehghani SM, Fallahi GH, Nejabat M. Cyclic vomiting syndrome in children: experience with 181 cases from southern Iran. *World J Gastroenterol* 2007 Mar 28; 13(12): 1833-36. [\[CrossRef\]](#)
13. Gokhale R, Huttenlocher PR, Brady L, Kirschner BS. Use of barbiturates in the treatment of cyclic vomiting during childhood. *J Pediatr Gastroenterol Nutr* 1997; 25: 64-7. [\[CrossRef\]](#)
14. Green M. *Pediatric Diagnosis*. 4th ed. Philadelphia: W. B. Saunders; 1986. p. 217.
15. Janin Y, Stone AM, Wise L. Mesenteric hernia. *Surg Gynecol Obstet* 1980; 150: 747-54.
16. Whitten DM, Feingold M, Eisenklam EJ. Hereditary pancreatitis. *Am J Dis Child* 1968; 116: 426-8. [\[CrossRef\]](#)
17. Silverman A, Roy C. *Pediatric Clinical Gastroenterology*. 3rd ed. St. Louis: C. V. Mosby; 1983. p. 851.
18. Green M. *Pediatric Diagnosis*. 4th ed. Philadelphia: W. B. Saunders; 1986. p. 219.
19. Fleisher DR. Cyclic vomiting syndrome and migraine. *J Pediatr* 1999; 134: 533-5. [\[CrossRef\]](#)
20. Mitchell WG, Greenwood RS, Messenheimer JA. Abdominal epilepsy. Cyclic vomiting as the major symptom of simple partial seizures. *Arch Neurol* 1983; 40: 251-2. [\[CrossRef\]](#)
21. Sarkari NB, Bickerstaff ER. Relapses and remissions in brain stem tumours. *Br Med J* 1969 Apr 5; 2: 21-3. [\[CrossRef\]](#)
22. Frank Y, Schwartz SB, Epstein NE, Beresford HR. Chronic dysphagia, vomiting and gastroesophageal reflux as manifestations of a brain stem glioma: a case report. *Pediatr Neurosci* 1989; 15: 265-8. [\[CrossRef\]](#)
23. Feldman M. Nausea and vomiting. In Slesinger M, Fordtran J, editors. *Gastrointestinal disease*. 4th ed. Philadelphia: W. B. Saunders; 1989. p. 227.
24. Valenzuela GA, Smalley WE, Schain DC, Vance ML, McCallum RW. Reversibility of gastric dysmotility in cortisol deficiency. *Am J Gastroenterol* 1987; 82: 1066-8.
25. Stackpole RH, Melicow MM, Uson AC. Pheochromocytoma in children. Report of 9 case and review of the first 100 published cases with follow-up studies. *J Pediatr* 1963; 63: 314-30.
26. Berry G. Disorders of the amino acid metabolism. In: Walker W, Durie P, Hamilton J, et al, editors. *Pediatric Gastrointestinal Disease*. Philadelphia: B. C. Decker; 1991. p. 948-50.
27. Coates PM, Hale DE, Stanley CA, Corkey BE, Cortner JA. Genetic deficiency of medium-chain acyl coenzyme A dehydrogenase: studies in cultured skin fibroblasts and peripheral mononuclear leukocytes. *Pediatr Res* 1985; 19: 671-6. [\[CrossRef\]](#)
28. Rezvani I, Auerbach VH. Propionic acidemia. In: Behrman R, Vaughn V, editors. *Nelson's Textbook of Pediatrics*. 13th ed. Philadelphia: W. B. Saunders; 1987. p. 292-3.
29. Sweetman L. Branched chain organic acidurias. In: Scriver C, Beaudet A, Sly W, et al, editors. *Metabolic basis of inherited disease*. 6th ed. New York: McGraw-Hill; 1989. p. 795.
30. Stein JA, Tschudy DP. Acute intermittent porphyria. A clinical and biochemical study of 46 patients. *Medicine (Baltimore)* 1970; 49: 1-16. [\[CrossRef\]](#)
31. Elder J, Duckett J. Dietl's crisis. In: Gillenwater J, Grayhack J, Howards S, et al, editors. *Adult and pediatric urology*. Chicago: Year Book Medical Publishers; 1987. p. 1555.
32. Koff SA, Hayden LJ, Cirulli C, Shore R. Pathophysiology of ureteropelvic junction obstruction: experimental and clinical observations. *J Urol* 1986; 136: 336-8.
33. Inal A, Yilmaz M, Kendirli SG, Altintas DU, Karakoc GB. The clinical and genetical features of 124 children with Familial Mediterranean fever: experience of a single tertiary center. *Rheumatol Int* 2009; 29: 1279-85. [\[CrossRef\]](#)
34. Gurkan OE, Fidan K, Dalgic B. Esophagitis and widespread aphthous ulcerations in gastric mucosa in an infant with familial Mediterranean fever. *J Pediatr Gastroenterol Nutr* 2014; 59: e11-3. [\[CrossRef\]](#)
35. Koletzko S, Jones NL, Goodman KJ, et al. Evidence-based guidelines from ESPGHAN and NASPGHAN for *Helicobacter pylori* infection in children. *J Pediatr Gastroenterol Nutr* 2011; 53: 230-43. [\[CrossRef\]](#)
36. Li BUK, Dumont RC, Kollman CE, et al. Is endoscopy with biopsies useful in the evaluation of chronic vomiting in childhood? *Gastroenterology* 1993; 104: A133.