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TECHNICAL NOTES

Chronic vomiting in children: Etiology, diagnosis, and management

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Introduction

Vomiting involves forceful expulsion of gastric contents through the mouth (may be associated with nausea and retching). Nausea is a subjective feeling of unpleasantness accompanied by pallor, hypersalivation, and anorexia. Retching encompasses spasmodic respiratory movements, and contraction of abdominal muscles against a closed glottis without actually throwing out gastric contents [1]. Regurgitation is the passive effortless movement of gastric contents into the mouth without abdominal wall contractions. Rumination involves effortless bringing up of recently ingested food through a voluntary increase in abdominal pressure, chewing, and sometimes re-swallowing [2]. Though definitions make our understanding easier, analyzing the symptoms in a child is a challenge in itself and a clear distinction between the above conditions cannot be made and the parents often put everything in the basket of "vomiting." Thus, tweezing out the underlying cause requires thorough history taking from the child and the parents. The next question that arises with respect to children is the definition of chronic vomiting. Though the ROME IV criteria define the duration of chronic nausea and vomiting in children as 2 months, a more practical cut-off would be to take 4 weeks so that evaluation is not delayed [3].

Etiology

The etiology of chronic vomiting in children is diverse, varies with age, and includes extraintestinal causes also. Differential diagnosis of chronic vomiting based on the age of the child is given in Table 1. The causes can be broadly divided into those arising due to gastrointestinal (GI), metabolic, endocrine, neurological, and renal disorders [4]. Many of the obstructive causes have a dramatic presentation, however, non-critical narrowing can present as chronic vomiting, failure to thrive, and feed refusal. If a congenital anomaly of the GI tract is diagnosed, other associated anomalies should be actively looked for because these may cause persistent symptoms despite surgical correction of the obstruction. Gastroesophageal reflux (GER) is a physiological phenomenon affecting 50% infants between 0 and 3 months, 67% in those between 4 and 6 months, and it decreases to 5% at 1 year [5]. Most of them are "happy spitters" and are otherwise normal. But 5% to 10% of them can have pathological gastroesophageal reflux disease (GERD) causing bothersome symptoms, failure to gain weight, or complications [6]. One of the manifestations of cow's milk protein allergy (CMPA) is recurrent vomiting and it can start in the first few days of birth after exposure to bovine milk protein [7]. In all babies with GERD, CMPA ought to be considered a possibility [8]. Eosinophilic esophagitis (EoE) is an emerging disease in children and 38% present with symptoms similar to GERD [9]. In infants and older children, apart from the other anatomical causes of obstruction, intussusception can present with vomiting in 48% cases along with pain and incessant crying [10]. Intestinal tuberculosis and Crohn's disease can have vomiting in 8% to 20% children [11]. In normal children and adolescents, at least one episode of rumination is seen in up to 11% and recurrent rumination in 1.5% [12].

Though metabolic causes can present acutely, many of them can have recurrent vomiting as the initial manifestation. Diagnosing these disorders urgently is imperative to initiate treatment. Any cause of raised intracranial pressure can present with vomiting. In children with intracranial tumors, 30% have vomiting as the earliest symptom along with headache [13]. Cyclical vomiting syndrome (CVS) prevalence in normal children is only 0.3% but it is important to recognize it as a specific cause of recurrent vomiting [14]. Renal and endocrine diseases may also have vomiting as the sole symptom. Many of the

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Table 1 Etiology of chronic vomiting in relation to the age of the child

Neonates	Infants	Children	Adolescents
Gastrointestinal			
Esophageal stenosis	GERD	GERD	Rumination syndrome
GERD	Cow's milk protein allergy	Cow's milk protein allergy	Gastritis
Cow's milk protein intolerance	Intestinal malrotation	Eosinophilic esophagitis	Peptic ulcer disease
Congenital microgastria	Duodenal web	Gastritis	Eosinophilic esophagitis
Hypertrophic pyloric stenosis	Esophageal stricture	Achalasia cardia	GERD
Duodenal web	Ileal jejunal stenosis	Esophageal, pyloric strictures	Esophageal, pyloric strictures
Intestinal malrotation	Intussusception	Foreign body ingestion	Achalasia cardia
Duplication cyst	Hirschsprung disease	Superior mesenteric artery syndrome	Crohn's disease
Annular pancreas	Annular pancreas	Crohn's disease	Intestinal tuberculosis
Ileal, jejunal stenosis	Very early onset inflammatory bowel disease	Intestinal tuberculosis	Gastrointestinal lymphoma
Hiatus hernia	Gastroparesis	Gastrointestinal lymphoma	Superior mesenteric artery syndrome
Hirschsprung disease	Duplication cyst	Rumination syndrome	Gastroparesis
Intestinal aganglionosis		Intestinal malrotation	Chronic pseudo-obstruction
		Intussusception	Distal intestinal obstruction syndrome
			Chronic pancreatitis
Metabolic			
Urea cycle defects	Hereditary fructose intolerance	Hereditary fructose intolerance	Urea cycle defects
Fatty acid oxidation defects	Urea cycle defects	Urea cycle defects	Fatty acid oxidation defects
Organic acidemias	Fatty acid oxidation defects	Fatty acid oxidation defects	Acute intermittent porphyria
Mitochondrial hepatopathies	Organic acidemias	Organic acidemias	
Gluconeogenic disorders	Mitochondrial hepatopathies	Mitochondrial hepatopathies	
Galactosemia			
Phenylketonuria			
Congenital lactic acidosis			
Endocrine			
Congenital adrenal hyperplasia	Hypercalcemia	Diabetic ketoacidosis	Diabetic ketoacidosis
Neonatal thyrotoxicosis	Addison disease	Hypercalcemia	Hypercalcemia
Hypercalcemia		Hyperthyroidism	Hyperthyroidism
		Addison disease	Addison disease
Neurological			
Congenital hydrocephalus	Intracranial tumors	Cyclical vomiting syndrome	Cyclical vomiting syndrome
Meningitis	Meningitis	Intracranial tumors	Intracranial tumors
Arnold–Chiari malformation	Pseudotumor cerebri	Meningitis	Meningitis
Intracranial hemorrhage		CNS tuberculosis	CNS tuberculosis
Pseudotumor cerebri		Neurocysticercosis	Neurocysticercosis
			Bulimia nervosa
			Functional vomiting
			Migraine
Others			
Hydronephrosis	UTI	Uremia	Uremia
UTI	Uremia	UTI	UTI
VUR	VUR	Hydronephrosis	Vestibular disorders
Neonatal abstinence syndrome	Renal tubular acidosis	Vestibular disorders	Cannabinoid hyperemesis syndrome
	Munchausen syndrome by proxy		Glaucoma

Table 1 (continued)

Neonates	Infants	Children	Adolescents
Munchausen syndrome by proxy			
			Drug induced
			Testicular/ovarian torsion

GERD gastroesophageal reflux disease, *CNS* central nervous system, *UTI* urinary tract infection, *VUR* vesicoureteric reflux

extraintestinal causes have a recurrent pattern of vomiting as that seen in CVS, organic acidemia, hydronephrosis, urea cycle defects, diabetic ketoacidosis, and Addison's disease. Intestinal malrotation with volvulus also may have a recurrent pattern. Most of the other causes have a chronic continuous pattern.

Diagnosis

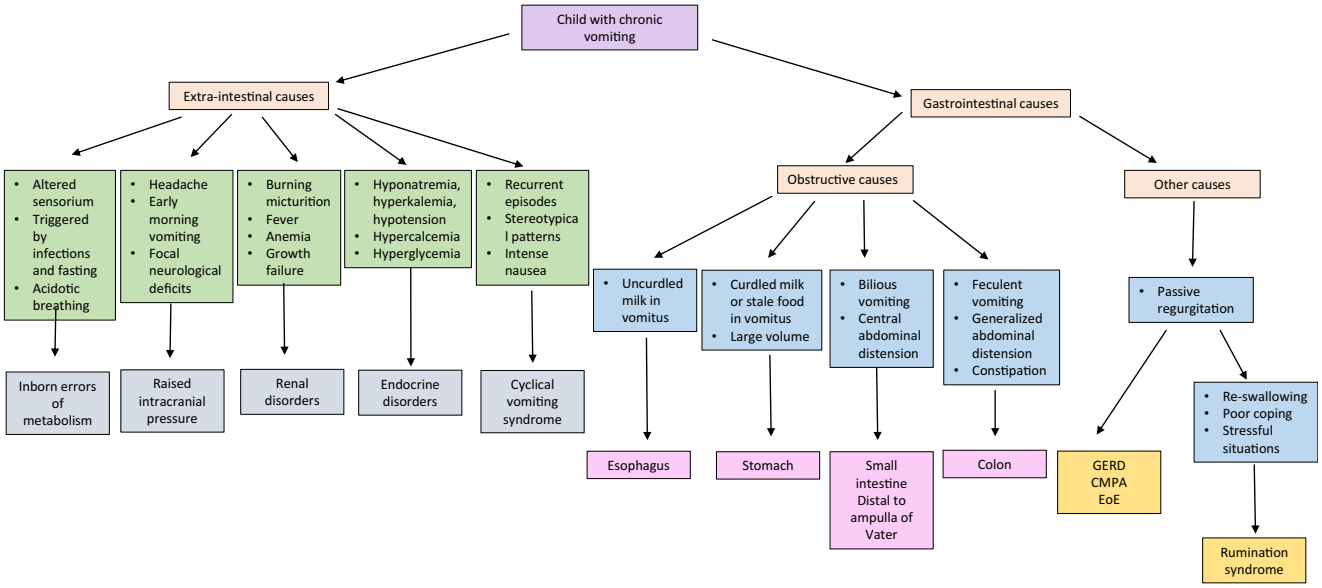
Arriving at a clinical diagnosis and tailoring investigations in a child with vomiting is akin to solving a jigsaw puzzle. In most of the cases, broad classification of etiology can be ascertained with clinical features and routine hematological investigations, which can be confirmed with specific tests. Clinical approach to a child with chronic vomiting is given in Fig. 1.

Step 1: gastrointestinal versus extraintestinal cause

Differentiating between GI and extraintestinal source is the foremost step. Children with raised intracranial pressure often present with early morning vomiting and headache. They may have focal neurological deficits, seizures, macrocephaly, and behavioral problems. Recurrent episodes of vomiting along with encephalopathy triggered by minor infections, acidosis, hypoglycemia, and hyperammonemia could indicate underlying inborn errors of metabolism. Vomiting can be induced by protein-rich diet in urea cycle defects and organic acidemia, sweets, and juices in hereditary fructose intolerance. Acute intermittent porphyria can present with vomiting in association with hypertension and peripheral neuropathy. Hyponatremia, hyperkalemia, hypotension, and ambiguous genitalia suggest congenital adrenal hyperplasia. Fever, burning micturition, anemia, growth failure, normal anion gap acidosis, elevated urea, and creatinine suggest renal disorders. CVS occurs in stereotypical patterns with absolute normalcy in between episodes and could be triggered by stressful events; there can be associated family history of migraine, and may be associated with intense nausea and frequency of vomiting may be as high as 4 times in 1 h [15]. Thus, basic metabolic workup will include arterial blood gas, lactate, electrolytes, blood glucose, arterial ammonia, liver enzymes, urea, creatinine, urine ketones, urine non-glucose reducing substances, and urine porphyrins.

Step 2: source in the gastrointestinal tract

Once the source is narrowed to the GI tract, the next step is to ascertain the location of pathology. In an infant, if the vomitus contains uncurdled milk, esophageal causes should be considered. If the vomitus is large in quantity, and contains curdled milk in infants or stale food in children, etiology is likely to be localized to the stomach. In congenital hypertrophic pyloric stenosis (CHPS), infants will present with non-bilious projectile vomiting from 2 to 8 weeks of life, an olive may be palpable in the right upper quadrant in half of them, and dehydration and metabolic alkalosis is seen in up to 30% [16]. CMPA can present with GERD, hematemesis, and refusal to feed. When anatomical obstruction is considered, the site of block ought to be determined. Non-bilious vomiting suggests obstruction proximal to ampulla of Vater, in bilious vomiting obstruction is likely to be distal to ampulla and feculent vomiting could suggest colonic stasis. Pain and visible bowel loops in the periumbilical area would suggest small intestinal obstruction, generalized distension, and obstipation would narrow the cause to the colon. Children with intussusception may have a sausage-shaped mass palpable in the right side of abdomen and "current jelly" stools [10]. Constitutional symptoms will accompany intestinal tuberculosis, Crohn's disease, and lymphoma. History of rapid weight loss preceding onset of vomiting is clue to superior mesenteric artery (SMA) syndrome. In rumination syndrome, regurgitation occurs immediately after eating, the act of vomiting can be controlled, and re-swallowing may also be present. In those with achalasia cardia, dysphagia is a predominant complaint along with regurgitation and nocturnal cough. In children who have dysphagia, vomiting, skin pigmentation, hypotension, hyperkalemia, and hypotension, possibility of Allgrove syndrome should be considered (achalasia cardia, adrenal insufficiency, and alacrimia).



GERD gastroesophageal reflux disease, *CMPA* Cow's milk protein allergy, *EoE* eosinophilic esophagitis

Fig. 1 Approach to a child with chronic vomiting

Step 3: specific investigations

Investigations ought to be planned based on the clinical diagnosis.

Radiological investigations

Erect radiographs ought to be performed if obstructive causes are suspected. In infant, single bubble and double bubble signs may be seen in pyloric and duodenal obstruction, respectively. Multiple air fluid levels may be seen on erect abdominal radiographs in other causes of intestinal obstruction. Ultrasonogram is diagnostic in CHPS (pyloric muscle wall thickness > 3 mm and pyloric canal length > 12 mm), gut duplication (gut signature sign), intussusception (target sign, pseudokidney sign, Doppler for vascularity), and malrotation with volvulus (relationship between superior mesenteric artery and vein) [17–19]. Upper GI series best demonstrates malrotation and other causes of anatomical obstruction. Timed barium swallow studies would show hold-up of the contrast in achalasia cardia. Contrast-enhanced computed tomography will be needed in cases with intestinal tuberculosis, Crohn's disease, GI lymphoma, and SMA syndrome.

Esophagogastroduodenoscopy

Of all children presenting to an endoscopy unit, 21% had persistent vomiting as the symptom [20]. The overall yield of esophagogastroduodenoscopy (EGD) in children with vomiting is 67% [21]. Conditions that can be diagnosed on EGD are esophageal strictures, foreign body, erosive esophagitis, EoE, peptic ulcer disease, gastritis, and gastric outlet obstruction. In EoE, EGD will show linear furrows, trachealization of esophagus, whitish plaques, mucosal fragility, small luminal caliber, and biopsy will demonstrate increase in eosinophils [22].

Manometry

High-resolution esophageal manometry can diagnose and classify achalasia cardia and other causes of esophageal dysmotility. However, in young children, placement of catheter will require mild sedation. Swallows should be given after the effect of sedation is worn off. For antroduodenal manometry, placement of catheter usually requires deeper anesthesia, which can affect digestive motility [23]. Extrapolating Chicago classification in children is complicated due to variations based on age and height [24]. There are limited indications for antroduodenal manometry in children which include gastroparesis, pseudo-obstruction, and rumination syndrome.

Others

CMPA is diagnosed by elimination of milk and milk products in the diet for 1 to 2 weeks, symptom resolution, and recurrence on re-challenge [7]. Twenty-four-hour pH-impedance monitoring for acid reflux, nuclear studies for gastric

emptying, breath tests for small bowel motility, and full thickness intestinal biopsy in pseudo-obstruction are specific tests that need to be done on a case-to-case basis. Bulimia nervosa, functional vomiting, rumination, migraine, and CVS are diagnosed clinically but often additional tests have to be performed to rule out organic etiology.

Management

Abnormalities such as dehydration, electrolyte imbalance, hypoglycemia, and acid balance need to be corrected primarily. Other management strategies depend on the underlying cause. Apart from medical and surgical management, endoscopic, dietary, and behavioral therapy are also a part of the therapeutic armamentarium in children with chronic vomiting. In case of obstructive causes, the child has to be kept nil orally; gastric decompression with nasogastric tube, intravenous fluids, and antibiotics have to be started followed by surgical consultation. In CMPA, therapeutic elimination of milk and milk products has to be done for a minimum of 6 months in IgE-mediated allergy and 12 to 18 months in non-IgE-mediated cases. In exclusively breast-fed babies, mother ought to eliminate milk products from her diet; if the baby is formula fed, extensively hydrolyzed formula (eHF) feeds should be given. Amino acid–based formula may be considered in severe cases not responding to eHF [25]. In babies with GERD, if there is no improvement after thickening feeds and elimination of milk, a 4 to 8-week trial of proton pump inhibitors (PPIs) should be given. In older children, if PPI trial is not successful or if weaning off PPI is difficult then EoE is a possibility. Following the six-food elimination diet (cow's milk, soy, egg, fish, wheat, nuts) can achieve remission 74% cases of EoE in 6 weeks [26]. Thereafter, sequential reintroduction will aid in identifying specific triggers. In the cohort that does not respond to PPI, viscous budesonide or oral fluticasone may have good efficacy [27]. In SMA syndrome, most improve with conservative management by hyperalimentation, nasojejunal feeding and only the resistant cases require duodenojejunostomy [28]. Pneumatic balloon dilatation has been the first line of treatment of achalasia followed by Heller's myotomy. Recently, there are many reports of successful per oral endoscopic myotomy in children [29]. Esophageal and pyloric strictures can be managed by endoscopic dilatations. Diaphragmatic breathing is the cornerstone of therapy in rumination syndrome. Other behavioral modifications like aversion techniques, general relaxation, and distraction may also be beneficial [30]. Making a positive diagnosis of CVS itself reduced the severity of vomiting in 78% children [31]. During the acute episode, abortive strategies include dextrose containing intravenous fluids, ondansetron, and sedation. Prophylactic measures comprise avoiding triggers, medications (first line: cyproheptadine, pizotifen [age $\leq$ 5 years] and amitriptyline [age > 5 years]), second line: propranolol), and supplements (carnitine and coenzyme Q) [15]. For gastroparesis, management includes low fat, low fiber, small frequent feeds, prokinetics (erythromycin, azithromycin, domperidone, metoclopramide, baclofen), and gastric electric stimulation, and in refractory cases botulinum toxin injection, pyloroplasty, or partial gastrectomy may be indicated [32]. In this issue, the article by Malik et al. has described the spectrum of chronic vomiting in children and has found rumination syndrome to be an important cause. Response to diaphragmatic breathing was demonstrated in 87% of them [33].

In conclusion, vomiting in children encompasses a whole gamut of causes. Reaching a clinical diagnosis guides further investigations for confirmation. Instead of searching for the needle in the haystack, a methodical approach will aid in making the right diagnosis and channelize the treatment.

Compliance with ethical standards

Conflict of interest AR declare that they have no conflict of interest.

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References

1. Lacy BE, Parkman HP, Camilleri M. Chronic nausea and vomiting: evaluation and treatment. Am J Gastroenterol. 2018;113:647–59.
2. Stanghellini V, Chan FK, Hasler WL, et al. Gastroduodenal disorders. Gastroenterology. 2016;150:1380–92.
3. Hyams JS, Di Lorenzo C, Saps M, Shulman RJ, Staiano A, van Tilburg M. Functional disorders: children and adolescents. Gastroenterology. 2016;S0016–5085:00181–5.
4. Parashette KA, Croffie J. Vomting. Pediatr Rev. 2013;34:307–19.
5. Nelson SP, Chen EH, Syniar GM, Christoffel KK. Prevalence of symptomatic gastroesophageal reflux during infancy. A pediatric practice-based survey, pediatric practice research group. Arch Pediatr Adolesc Med. 1997;151:569–72.
6. Hegar B, Dewanti NR, Kadim M, Alatas S, Firmansyah A, Vandenplas Y. Natural evolution of regurgitation in healthy infants. Acta Paediatr. 2009;98:1189–93.
7. Nielsen RG, Bindslev-Jensen C, Kruse-Andersen S, Husby S. Severe gastroesophageal reflux disease and cow milk hypersensitivity in infants and children: disease association and evaluation of a new challenge procedure. J Pediatr Gastroenterol Nutr. 2004;39:383–91.
8. Rosen R, Vandenplas Y, Singendonk M, et al. Pediatric gastroesophageal Reflux Clinical Practice Guidelines: Joint Recommendations of the North American Society for Pediatric Gastroenterology, Hepatology, and Nutrition and the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition. J Pediatr Gastroenterol Nutr. 2018;66:516–54.
9. Kapel RC, Miller JK, Torres C, Aksoy S, Lash R, Katzka DA. Eosinophilic esophagitis: a prevalent disease in the United

States that affects all age groups. Gastroenterology. 2008;134: 1316–21.
10. Zhao L, Feng S, Wu P, Lai XH, Lv C, Chen G. Clinical characteristics and surgical outcome in children with intussusceptions secondary to pathologic lead points: retrospective study in a single institution. Pediatr Surg Int. 2019;35:807–11.
11. Singh SK, Srivastava A, Kumari N, Poddar U, Yachha SK, Pandey CM. Differentiation between Crohn disease and intestinal tuberculosis in children. J Pediatr Gastroenterol Nutr. 2018;66:e6–e11.
12. Hartmann AS, Poulain T, Vogel M, Hiemisch A, Kiess W, Hilbert A. Prevalence of pica and rumination behaviors in German children aged 7-14 and their associations with feeding, eating, and general psychopathology: a population-based study. Eur Child Adolesc Psychiatry. 2018;27:1499–508.
13. Stocco C, Pilotto C, Passone E, et al. Presentation and symptom interval in children with central nervous system tumors. A single-center experience. Childs Nerv Syst. 2017;33:2109–16.
14. Bhatia V, Deswal S, Seth S, Kapoor A, Sibal A, Gopalan S. Prevalence of functional gastrointestinal disorders among adolescents in Delhi based on Rome III criteria: a school-based survey. Indian J Gastroenterol. 2016;35:294–8.
15. 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.
16. Bakal U, Sarac M, Aydin M, Tartar T, Kazez A. Recent changes in the features of hypertrophic pyloric stenosis. Pediatr Int. 2016;58: 369–71.
17. Costa Dias S, Swinson S, Torrão H, et al. Hypertrophic pyloric stenosis: tips and tricks for ultrasound diagnosis. Insights Imaging. 2012;3:247–50.
18. Sangüesa NC, Salvador LR, Palacios CE, Picó Aliaga S, Ibañez PV. Enteric duplication cysts in children: varied presentations, varied imaging findings. Insights Imaging. 2018;9:1097–106.
19. Bartocci M, Fabrizi G, Valente I, Manzoni C, Speca S, Bonomo L. Intussusception in childhood: role of sonography on diagnosis and treatment. J Ultrasound. 2014;18:205–11.
20. Thomson M, Sharma S. Diagnostic yield of upper and lower gastrointestinal endoscopies in children in a tertiary Centre. J Pediatr Gastroenterol Nutr. 2017;64:903–6.
21. El-Mouzan MI, Al-Mofleh IA, Abdullah AM, Al-Rashed RS. Indications and yield of upper gastrointestinal endoscopy in children. Saudi Med J. 2004;25:1223–5.
22. Muir AB, Merves J, Liacouras CA. Role of endoscopy in diagnosis and management of pediatric eosinophilic esophagitis. Gastrointest Endosc Clin N Am. 2016;26:187–200.
23. Rosen R, Garza JM, Tipnis N, Nurko S. An ANMS-NASPGHAN consensus document on esophageal and antroduodenal manometry in children. Neurogastroenterol Motil. 2018;30. https://doi.org/10.1111/nmo.13239.
24. Singendonk MM, Kritas S, Cock C, et al. Applying the Chicago Classification criteria of esophageal motility to a pediatric cohort: effects of patient age and size. Neurogastroenterol Motil. 2014;26: 1333–41.
25. Koletzko S, Niggemann B, Arato A, et al. Diagnostic approach and management of cow's-milk protein allergy in infants and children: ESPGHAN GI Committee practical guidelines. J Pediatr Gastroenterol Nutr. 2012;55:221–9.
26. Kagalwalla AF, Sentongo TA, Ritz S, et al. Effect of six-food elimination diet on clinical and histologic outcomes in eosinophilic esophagitis. Clin Gastroenterol Hepatol. 2006;4:1097–102.
27. Aceves SS, Bastian JF, Newbury RO, Dohil R. Oral viscous budesonide: a potential new therapy for eosinophilic esophagitis in children. Am J Gastroenterol. 2007;102:2271–9.
28. Sinagra E, Raimondo D, Albano D, et al. Superior mesenteric artery syndrome: clinical, endoscopic, and radiological findings. Gastroenterol Res Pract. 2018;27:1937416.
29. Lee Y, Brar K, Doumouras AG, Hong D. Peroral endoscopic myotomy (POEM) for the treatment of pediatric achalasia: a systematic review and meta-analysis. Surg Endosc. 2019;33:1710–20.
30. Murray HB, Juarascio AS, Di Lorenzo C, Drossman DA, Thomas JJ. Diagnosis and treatment of rumination syndrome: a critical review. Am J Gastroenterol. 2019;114:562–78.
31. Fitzpatrick E, Bourke B, Drumm B, Rowland M. Outcome for children with cyclical vomiting syndrome. Arch Dis Child. 2007;92:1001–4.
32. Setia A, Nair P, Cheng SX. Gastric electrical stimulation: an emerging therapy for children with intractable gastroparesis. World J Gastroenterol. 2019;25:6880–9.
33. Malik R, Srivastava A, Yachha SK, Poddar U. Chronic vomiting in children: a prospective study reveals rumination syndrome is an important etiology that is underdiagnosed and untreated. Indian J Gastroenterol. 2020;39: https://doi.org/10.1007/s12664-020-01025-y.