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Esophageal motility disorders in children with dysphagia: the utility of the Chicago classification

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ABSTRACT

Background: esophageal manometry is the standard criterion for the evaluation of dysphagia and the diagnosis of a primary motor disorder of the esophagus in adults and children.

Aims: to describe the diagnosis according to the Chicago classification (CC) v3.0 in children with dysphagia, in whom an esophageal motility disorder was documented. The associated comorbidities were also determined.

Methods: an observational retrospective study was performed of 54 patients evaluated for dysphagia, who had undergone a high-resolution manometry (HREM).

Results: a normal HREM was found in 52 % (n = 28) of the children, whereas 48 % (n = 26) had some esophageal motility disorder. The most frequent diagnosis was ineffective esophageal motility and achalasia. Excluding previously healthy children,

most children had a history of autoimmune disease and intellectual disability.

Conclusions: an esophageal motor disorder can be diagnosed in nearly half of infants and children with dysphagia. In this study, all esophageal diseases could be classified according to the CC v3.0. HREM should be considered for the evaluation of children with dysphagia, in addition to other studies.

Keywords: Dysphagia. High-resolution manometry. Ineffective esophageal motility. Achalasia.

INTRODUCTION

The evaluation of esophageal motility disorders in childhood can present a diagnostic challenge due to the diversity of clinical presentation. Esophageal dysphagia is a commonly referred symptom in pediatric gastrointestinal motility units and is present in up to 87 % of the children in whom a high-resolution esophageal manometry (HREM) is performed (1). HREM is often indicated in children with an anatomical obstruction or other well-defined problems that do not explain the dysphagia. Esophageal manometry is widely considered as the gold standard to assess esophageal motility. This technique provides detailed information about the esophageal pressure pattern as well as the sphincter function (2).

The Chicago classification (CC) of esophageal motility disorders has been widely used in the diagnosis of esophageal diseases in the adult and pediatric population and was based on metrics derived from studies in asymptomatic adult subjects (3,4). However, there are a few studies to characterize esophageal motility disorders in the pediatric population using the current CC. The aim of this study was to describe the characterization of esophageal motility disorders in children with dysphagia according to the current CC v3.0 and to describe the associated comorbidities in children with a diagnosed esophageal motility disorder.

METHODS

Patients

A retrospective, analytical and observational study was performed between January 2017 and February 2019. Inclusion criteria were: consecutive pediatric patients (age 0-18 years) referred for esophageal dysphagia to the physiology and gastrointestinal motility unit in the Instituto Nacional de Pediatría (Mexico City, Mex) were included, after a thorough evaluation by a pediatric gastroenterologist. All the patients underwent a superior digestive endoscopic study. Some patients underwent a contrasted barium esophagogram.

Exclusion criteria were: patients who did not complete the complete esophageal manometry protocol (registry of fewer than ten swallows) and incomplete data in the manometry records, history of anatomic malformation or esophageal surgery.

The presence or absence of gastrointestinal symptoms associated with esophageal dysphagia (abdominal pain, gastroesophageal reflux, nausea, vomiting and weight loss) was evaluated. Endoscopic esophagitis was established according to the Los Angeles classification.

High-resolution esophageal manometry

The HREM was performed after obtaining informed consent/assent of the parents and underage children, respectively. It was performed using a high-resolution impedance manometry system (Sandhill Scientific Inc., Highlands Ranch, CO, USA), recording ten effective drinks of 0.9 % saline at room temperature, according to the American Neurogastroenterology and Motility Society - North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (ANMS-NASPGHAN) recommendations (5). Manometric data were analyzed automatically using the BioView Analysis Sandhill Scientific software and then each study was reviewed manually. The probe had 32 circumferential pressure sensors spaced 1 cm apart and 16 impedance channels with a 2-cm spacing.

According to the patient's age, studies were performed with the patients in a recumbent position or being held in the semi-upright positions. The manometry catheter was placed nasally, with a simple lubricating gel, after a fast of six to eight hours and without sedation. The catheter was fixed once the lower esophageal

sphincter and/or esophagogastric junction was identified.

Data analysis

The manometric diagnosis was based using the CC algorithm (4). According to this algorithm, the first assessment of esophageal motility is whether there is an esophagogastric junction (EGJ) outflow obstruction as defined by integrated relaxation pressure (IRP). Disorders of EGJ obstruction are then further classified into achalasia subtypes and EGJ outflow obstruction. The next step was to look for major disorders of peristalsis, which included distal esophageal spasm (defined as normal IRP and ≥ 20 % of premature contractions distal latency < 4.5), hypercontractile esophagus (defined as ≥ 20 % of swallows with a distal contractile integral [DCI] > 8,000) and absent contractility (defined as normal EGJ relaxation with 100 % failed peristalsis). The final step was to look for minor disorders of peristalsis classified as ineffective esophageal motility, defined by a DCI < 450 mmHg-s-cm with ≥ 50 % ineffective swallows. Patients who did not demonstrate any of these disorder subtypes were classified as normal.

Statistical analysis

The inferential and descriptive statistics for the numerical values were shown as the mean and the categorical variables as percentages. The Mann-Whitney test was used to compare the total number of symptoms among patients with normal HREM *versus* abnormal HREM and the Chi-squared test was used to establish an association between esophagitis and abnormal manometry. The level of statistical significance was set at 0.05. Statistical evaluations were performed with the statistical software SPSS version 22 (IBM, Armonk, NY, USA). Statistical significance was considered when an alpha error value was < 0.05.

The study was performed in accordance with the Declaration of Helsinki.

RESULTS

Fifty-four patients who underwent HREM were included in the study; 52 % (n = 28) had a normal HREM and 48 % (n = 26) had some manometry alteration, according to the CC

of esophageal motility disorders v3.0. The median age was 10.4 years (range 1-17 years); 50.9 % were female and 49.1 % were male.

The main symptoms observed in addition to dysphagia were abdominal pain in 44 %, reflux (regurgitation/heartburn) in 44 %, nausea in 33 %, vomiting in 26 % and weight loss in 16 %. There were no differences in the total number of symptoms among patients with normal HREM *versus* abnormal HREM (p = 0.90).

In addition, 42.6 % (n = 23) of patients were previously healthy and only had dysphagia with any of the symptoms previously mentioned. The group of autoimmune diseases represented 20.4 % (n = 11) of the children evaluated, followed by 16.6 % of patients with intellectual disability (n = 9). Patients with congenital gastrointestinal malformations, oncological diseases and allergic diseases each represented 5.5 %; the rest of the associated comorbidities are presented in table 1.

Esophagitis was found in 39 % (11/28) of children with a normal esophageal manometry during the endoscopic evaluation, whereas it was documented in 30 % (8/26) of children with an abnormal manometry. This difference was not significant (p = 0.58).

The most frequent manometric finding according to the CC v3.0 (Table 2) were ineffective esophageal motility in 37 %, followed by EGJ outflow obstruction in 14.8 %. Jackhammer esophagus and distal esophageal spasm were found in 3.7 %.

DISCUSSION

Esophageal dysphagia in children is one of the most common causes of presentation in the gastrointestinal motility unit. In our study, all pediatric patients with some esophageal motor disorder could be classified according to the algorithm of the CC v3.0. The classification and application of esophageal motor disorders in pediatric patients have evolved over the years. Singendonk et al. reported a retrospective study that applied the 2012 CC criteria, and the esophageal motility disorders in children were classified in 65.8 %. They found that CC metrics, particularly IRP and distal latency, were age and size-dependent and required an adjustment to improve the accuracy of diagnosis in children (6). Recently, a prospective study reported that

certain HREM metrics were substantially influenced by the esophageal length and required adjusted diagnostic thresholds, specifically for children (7). However, Edeani et al. showed that esophageal motor disorders in children could be identified in all cases using the current CC, which is similar to our study (1).

The symptoms of abnormal esophageal motility in children are like those in adults, although symptoms are usually reported by the parents for younger children. The presenting complaints can range from chest pain and dysphagia to pyrosis, regurgitation, heartburn, nausea, vomiting and poor eating, which can potentially lead to malnutrition. The spectrum of symptoms reported in our study is similar to that described in other studies with pediatric patients (8,9).

We found that children with some autoimmune disease frequently had some esophageal motor disorder. Dysphagia is a common symptom in patients with rheumatologic diseases (10) and patients with achalasia are 3.6 times more likely to suffer from any autoimmune condition (11). Immunological diseases are increasingly frequent in the pediatric age (12). Thus, it is important to evaluate the esophageal motility in the presence of dysphagia.

Intellectual disabilities were secondary to Down's syndrome in the majority of our cases and up to 63.8 % of children with Down's syndrome may have dysphagia (13). Zárate et al. reported that esophageal motor disorders, particularly achalasia, are frequent in individuals with Down's syndrome (14). Oropharyngeal dysphagia is a common diagnosis in children with cerebral palsy (15). Nevertheless, esophageal dysphagia is not evaluated frequently and therefore its prevalence in these patients is unknown.

Esophageal dysmotility is almost universal after esophageal atresia repair and is mainly related to a developmental anomaly of the esophagus (16). Aperistalsis is the most frequent finding in the HREM and gastroesophageal reflux-related symptoms are frequently reported (17). Dysphagia is a very unusual symptom of duodenal atresia (18), possibly associated to gastroesophageal reflux disease (19).

In patients with acute leukemia, dysphagia is usually related to infection, gastroesophageal reflux, chemotherapy toxicity or benign strictures (20). However,

there are no studies that characterize esophageal motility in patients with dysphagia and oncohematologic disease. Therefore, future studies will define the frequency and type of manometric alterations in this group of patients.

The prevalence of childhood food allergies has increased. The most frequent gastrointestinal symptoms include nausea, vomiting, diarrhea and pain (21). Dysphagia is not a frequent symptom in children with a food allergy and may occur in patients with eosinophilic esophagitis, and is less often associated with a cow's milk protein allergy (22). The pathophysiological mechanisms of the dysphagia in patients with eosinophilic esophagitis are multifactorial. Primary motility disorders such as achalasia or diffuse esophageal spasms, as well as non-specific motility disorders including abnormal peristalsis and high amplitude contractions have also been described (23,24). An association between a food allergy and gastroesophageal reflux disease was observed in nearly half of infants and children (25). In fact, it has been postulated that chronic exposure to acid can affect esophageal motility, although pediatric studies are still inconclusive (26). In our study, there were three patients with a history of allergy and dysphagia. The child with eosinophilic esophagitis had a manometric diagnosis of ineffective esophageal motility and the two children with a cow's milk protein allergy had a normal manometry.

In our study, a high frequency of achalasia was found, although it has been reported as a disease with low prevalence in the pediatric age (27). Our findings are probably explained by the fact that our unit is one of the few centers in the country where HREM is performed in pediatric patients. We also found a high frequency of minor disorders, specifically ineffective esophageal motility. This is a heterogeneous disorder and not consistently related to disease states or symptoms and may also be associated with gastroesophageal reflux disease (28). Future studies in children should define the factors associated with the development of this entity.

There are some limitations related to the current study. First, this was a retrospective study and there is a limited number of patients. In addition, the symptoms reported in the study were sometimes perceived by the caregiver in instances where the patient could not verbalize symptoms. Due to the findings of the influence of esophageal

length on HREM metrics, the clinical context of the patients should be extensively evaluated, with the support of radiological and endoscopy studies that contribute to an accurate diagnosis.

CONCLUSIONS

The CC v3.0 offers a systematic approach for the diagnosis of esophageal motility disorders in adults and can be used to diagnose these diseases in the pediatric population. In our study, an esophageal motor disorder could be characterized in nearly half of infants and children with dysphagia. The most frequent manometric findings according to the CC v3.0 were ineffective esophageal motility and achalasia. Therefore, the performance of a HREM should be considered in the evaluation of children with esophageal dysphagia.

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Table 1. Patient characteristics and comorbidity conditions in pediatric patients with esophageal dysphagia

Characteristics and comorbid conditions	*% (n = 54)*
Median age (years)	10.4 (range 1-17)
Median female	52 % (28)
Previously healthy	42.6 % (23)
Autoimmune diseases*	20.4 % (11)
Intellectual disability[†]	16.6 % (9)
Congenital malformations of gastrointestinal tract[‡]	5.5 % (3)
Oncological diseases[§]	5.5 % (3)
Allergic diseases[‖]	5.5 % (3)
Eating disorders[¶]	1.8 % (1)
Fundoplication	1.8 % (1)

*Systemic lupus erythematosus, scleroderma, dermatomyositis, autoimmune thyroiditis. [†]Down's syndrome, cerebral palsy. [‡]Duodenal atresia. [§]Acute lymphoblastic leukemia. [‖]Eosinophilic esophagitis, Cow's milk protein allergy. [¶]Anorexia.

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Table 2. Diagnosis of esophageal motility disorders in pediatric patients with dysphagia based on the Chicago Classification v3.0

Disorders	*% (n = 26)*
Ineffective esophageal motility	38.4 (10)
Achalasia	38.4 (10)
Type 1	3.8 (1)
Type 2	26.9 (7)
Type 3	7.6 (2)
EGJ outflow obstruction	15.4 (4)
Jackhammer esophagus	3.8 (1)
Distal esophageal spasm	3.8 (1)

EGJ: esophagogastric junction.