Association between Eosinophilic Esophagitis and Esophageal Food Impaction in the Pediatric Population

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Abstract

Objectives. (1) To describe the presentation, management, and outcomes associated with pediatric esophageal food impaction (EFI) at a single tertiary care institution. (2) To identify the key clinical features of pediatric EFI that are associated with a diagnosis of eosinophilic esophagitis (EoE).

Study Design. Case series with chart review.


Subjects and Methods. Thirty-five children <18 years of age presenting with EFI between November 1, 2006, and October 31, 2013, were included. Presenting symptoms, medical history, biopsy results, endoscopic findings, and underlying etiology were examined. Fisher exact test, t tests, and logistic regression were used to compare between patients with and without EoE.

Results. Thirty-five patients had isolated EFI and were included in the study. EoE accounted for 74% (n = 26) of pediatric EFI, with the remaining cases being attributed to neurologic impairment (n = 5, 15%), prior surgeries (n = 1, 3%), reflux esophagitis (n = 1, 3%), or unknown etiologies (n = 2, 6%). EFI was the initial manifestation of EoE in 81% (n = 21) of patients. The most common presenting symptoms were dysphagia (n = 34), choking (n = 26), and vomiting (n = 23). Linear furrowing was the only endoscopic finding that was significantly associated with EoE (P < .001).

Conclusion. Most esophageal food impactions in the pediatric population are associated with an underlying diagnosis of EoE and are often the initial manifestation of the disease. EoE must be considered in all pediatric patients with EFI; esophageal biopsies should be strongly considered in these patients at the time of endoscopic management of the EFI.

Keywords

esophageal food impaction, esophageal foreign bodies, eosinophilic esophagitis, dysphagia

Eosophageal foreign body impaction is a common clinical scenario faced by physicians treating pediatric and adult patients. In a large retrospective study, the estimated annual incidence of esophageal foreign body impaction was 13.0 per 100,000.1 Food bolus impactions, typically consisting of meat products, represent most esophageal foreign body cases in adults and comprise a significant subset of those in the pediatric population.2,3 A recent epidemiological review of 548 cases of esophageal foreign body impactions identified that 63% of adult cases were secondary to food products.2 In the United States and Canada, esophageal food impaction (EFI) is responsible for 9% to 13% of pediatric esophageal foreign body ingestions based upon a recent systematic review.4 EFI in adults is most frequently attributed to underlying anatomic abnormalities: benign strictures, peptic ulcer disease, and previous surgical anastomoses.3,5 In children, however, there is an increasing body of evidence to suggest that chronic esophageal inflammation and motility disorders play a more prominent role in EFI than structural defects.5 Recently, eosinophilic esophagitis (EoE) has been identified as one of the key pathologic entities responsible for the majority of pediatric EFI.2,5

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Although a tissue biopsy is required to make the diagnosis of EoE, several endoscopic findings are associated with this disease process: linear furrowing, white exudates, linear shearing with passage of the endoscope, and strictures. While none of these endoscopic features are pathognomonic for EoE, the presence of 1 or more of the above findings in the appropriate clinical context is strongly suggestive of the diagnosis.

Despite the increasing body of evidence demonstrating that EoE is responsible for a significant percentage of pediatric food impactions, the importance of obtaining esophageal biopsies in the workup for EFI, especially if the esophagus appears grossly normal, remains uncertain. The goals of the current study were (1) to describe the presentation, management, and outcomes associated with pediatric EFI at a single tertiary care institution and (2) to identify the key clinical and endoscopic features of pediatric EFI that are predictive of a diagnosis of EoE.

Methods
This study was reviewed by the University of Pittsburgh Institutional Review Board and approved by expedited review. A case series with chart review was conducted using the Children’s Hospital of Pittsburgh of UPMC inpatient and outpatient hospital databases to identify all patients who presented to the emergency department with EFI between November 1, 2006, and October 31, 2013. Patients were identified by searching our medical record databases using the International Classification of Diseases, Ninth Revision (ICD-9) code for the diagnosis of foreign body of the esophagus (935.1). We also included patients who underwent rigid or flexible esophagoscopy for removal of a foreign body by searching based on Current Procedural Terminology (CPT) codes for esophagoscopy with removal (43194, 43215). The search was then limited to patients with EFI. Inclusion criteria consisted of all patients with EFI. Exclusion criteria included patients older than 21 years and those with simultaneous nonorganic esophageal impactions.

Data were collected and placed into a spreadsheet using deidentified information. The collected data included age at presentation, sex, presenting symptoms, endoscopic findings, medical history, family history of atopy, esophageal biopsy results, and complications. EoE was diagnosed if a biopsy specimen had >15 eosinophils/high-powered field (HPF). Once all information was collected, the data were tabulated for statistical analysis. Fisher exact tests, $t$ tests, and logistic regression were used to compare patients with an underlying diagnosis of EoE to those with neurological impairment, prior surgeries, or unknown causes. Statistical significance was defined as a $P$ value less than .05. SAS 9.4 (SAS Institute, Cary, North Carolina) was used to conduct all statistical analyses.

Results
During the study period, 48 patients presented to the emergency department (ED) with an esophageal food impaction. However, 13 of these patients had a second foreign body along with the food impaction (most commonly a coin) and were excluded from the study. Of the 35 patients in the study population, the mean age was 12.3 years, the median age was 12.9 years, and 26 patients (74%) were male. Meat products accounted for most EFI cases (n = 32): beef (n = 13), chicken (n = 9), hotdog (n = 3), meatball (n = 3), and pork (n = 4). Nonmeat products included carrots (2) and pretzels (1). The most common presenting symptoms were dysphagia (n = 34, 97.1%), choking (n = 26, 74.3%), vomiting (n = 23, 65.7%), and drooling (n = 23, 65.7%).

Flexible endoscopy was used in 21 cases (60%) while rigid instrumentation was used in the remaining 14 patients (40%). Three main services were involved in the management of food bolus impactions at our institution: pediatric gastroenterology (n = 20, 57%), pediatric otolaryngology (n = 14, 40%), and pediatric general surgery (n = 1, 3%). Of note, the pediatric otolaryngology service relied upon rigid instrumentation while the pediatric gastroenterology and pediatric general surgery services used flexible endoscopy for food bolus removal. Both flexible and rigid endoscopy were successful in relieving impaction without serious complications. Thirty patients (86%) received an esophageal biopsy at the time of food bolus removal. Of the 5 patients who were not biopsied, 4 had a history of neurologic impairment that was attributed to the EFI event. It remains unclear why the remaining patient did not receive a diagnostic biopsy. Complications associated with food impaction included esophageal abrasion (n = 4, 11.4%), mucosal irritation (n = 5, 14.3%), and esophageal edema/erythema (n = 15, 42.9%). There were no cases of esophageal perforation. All complications were self-resolving, and patients rapidly recovered following bolus removal.

Etiology of EFI
Etiology of patients’ EFI was grouped into 4 major subdivisions: EoE, neurologic impairment/motility disorders, prior surgeries, and other/unknown (Table 1). Esophageal biopsies were obtained in 30 patients (86%), and only 4 cases demonstrated normal histology. The most common etiologies noted in our review were EoE (n = 26, 74%) and history of neurological impairment/motility disorders (n = 5, 14%). The remaining 4 cases included patients with prior esophageal surgery due to esophageal perforation from button battery impaction (n = 1, 3%), significant reflux esophagitis (n = 1, 3%), or unknown etiologies (n = 2, 6%). Of the 30 of 35 patients who had a biopsy conducted, 26 (87%) were diagnosed with EoE. Six of 35 patients (17%) had normal findings on esophagoscopy (no linear furrowing, trachealization, cobblestoning, or evidence of inflammation). Four of these 6 patients had esophageal biopsies, and half (2/4) were diagnosed with EoE on biopsy. Table 1 enumerates the clinical characteristics, history, physical exam, radiologic, and endoscopic findings in patients with EFI by etiology.

Characteristics of Patients with EoE
Certain clinical variables did affect a patient’s odds of having a diagnosis of EoE. Endoscopic evaluation was
conducted on all patients who presented with EFI at the time of removal. Linear furrowing on endoscopy increased the odds of the patient having EoE (odds ratio [OR] = 26.66; confidence interval [CI], 2.75-258.07; \( P < .001 \)), whereas cobblestoning and trachealization were relatively uncommon and nonspecific findings. A 1-year increase in age led to a 34% increase in the odds of the patient having EoE (OR = 1.34; CI, 1.03-1.73; \( P = .03 \)). The odds ratio of having EoE between patients with a family history of atopy to those without was 6.86 (CI, 0.75-62.69; \( P = .09 \)), although this finding was not statistically significant. A forward stepwise method was used to build a multivariable logistic regression model to predict the presence of EoE. In separate models adjusting for linear furrowing, age was no longer significant and family history of atopy remained nonsignificant. Linear furrowing retained its significance in each model. As such, it was the only variable left in the final model predicting a patient having EoE.

Most patients diagnosed with EoE underwent skin prick allergy testing (\( n = 20, 77\% \)), and 15 of 20 (75%) had a positive reaction to multiple food allergens. In 17 of 20 (85%) of these cases, the skin prick allergy testing was performed after the EFI. The most common allergies noted were to milk (\( n = 8 \)), nuts (\( n = 8 \)), and eggs (\( n = 7 \)). Eosinophilic microabscesses were noted in the biopsy specimens of 8 patients with EoE. Of the patients with a diagnosis of EoE,
21 (81%) were newly diagnosed at the time of food impaction based on esophageal biopsy results. Among the newly diagnosed EoE patients, 18 of 26 patients (86%) had a history of allergies and 12 (57%) had a positive allergy test. Nearly half of all patients with a new diagnosis of EoE (n = 10, 47.6%) had a previous food impaction but did not receive a definitive diagnosis of underlying EoE at the time of the initial event. Five patients (19%) already had a known history of EoE at the time of endoscopy for EFI, and 4 of these 5 patients (80%) had had prior EFI episodes. None of these 5 patients were receiving optimal therapy for their EoE; 4 of the patients had been prescribed swallowed corticosteroid therapy but were noncompliant, and 1 patient was not on any treatment for the EoE.

**Discussion**

The current study attempts to examine the underlying etiology, complications, and management of pediatric EFI at a single tertiary care institution. Based on our analysis, most cases of EFI in our select population are associated with EoE, with a small minority being associated with neurologic impairment, motility disorders, or prior surgeries. These results closely parallel other recent studies that have identified EoE as the leading cause in pediatric EFI. For example, a systematic review and meta-analysis of EoE in children noted that the prevalence of EoE among children who had esophagogastroduodenoscopies (EGDs) performed for EFI was 63% to 88%. In fact, this study also noted that the incidence and prevalence of EoE have increased by 12% to 17% and 56%, respectively, over the past few decades. The authors concluded that the increase in EoE over time in children was a direct result of increased recognition by clinicians. The importance of EoE represents a paradigm shift in our understanding of pediatric EFI, as it was previously thought that Schatzki’s rings/peptic strictures were the primary etiology. Although a personal and family history of atopy may potentially be correlated with a diagnosis of EoE, these variables did not reach statistical significance in our analysis. Routine laboratory work was unremarkable in our patient cohort; however, a subset of patients with EoE had positive allergy testing to common food products, including milk and nuts. These data suggest that a personal or family history of allergies cannot be used to accurately risk stratify patients to determine if esophageal biopsies should be obtained. In fact, of the patients with EoE who underwent allergy testing, 25% had no documented reaction to common food products. Linear furrowing on endoscopic examination was significantly associated with EoE and should prompt physicians to strongly consider the diagnosis if noted on endoscopy. Although endoscopic findings may suggest a diagnosis of EoE, esophageal biopsies are still indicated to make a definitive diagnosis. Despite the importance of EoE in pediatric EFI, nearly half of the patients who were newly diagnosed with EoE had a previous food bolus impaction but were never diagnosed at that time. These findings reiterate that esophageal biopsies have not been considered a part of the standard workup for EFI.

Our results suggest that history, physical examination, allergy testing, and endoscopic findings are poor tools to accurately determine if patients with EFI require esophageal biopsies. Consequently, we recommend that all pediatric patients with EFI undergo multilevel esophageal biopsies to definitively test for EoE.

Even though the pathogenesis of EoE remains poorly understood, the underlying immune mechanisms are thought to involve both immediate and delayed hypersensitivity reactions that are classically associated with atopic disorders. In patients with EoE, esophageal eosinophils are activated by ingested/inhaled allergens and release key proinflammatory cytokines and oxygen free radicals that damage the surrounding mucosa. This chronic inflammation leads to ongoing tissue remodeling and the development of strictures, worsening dysphagia, and refractory gastroesophageal reflux disease (GERD). EFI is a known complication of EoE and is thought to be mediated by esophageal dysmotility, chronic inflammation, and esophageal remodeling. The importance of allergic hypersensitivity reactions in the progression of EoE is further highlighted by the fact that patients who eliminate trigger allergens from their diet often undergo complete remission. By accurately and rapidly diagnosing EoE, physicians can intervene at an earlier stage in the disease process to prevent downstream complications, including repeat food impactions and esophageal perforation.

Although there has been increasing research to support the importance of EoE in pediatric EFI, it remains unclear how important anatomic abnormalities and neurologic impairment are in this population. In one series of 43 patients, Diniz and Towbin demonstrated that EoE accounted for the majority of EFI cases (53%) but also noted that a large subset of patients with EFI (26%) had undergone prior surgery for esophageal atresia repair. In contrast to these results, our study identified underlying motility disorders as the second leading cause of EFI. The risk of EFI in patients with prior esophageal surgery and underlying motility disorders has yet to be clearly defined and requires further investigation as they are responsible for a notable subset of EFI cases.

The study has certain inherent limitations due to its retrospective nature. The small sample size of our population limited the ability to test for statistical significance in some variables. Furthermore, the population we studied was limited to a single tertiary care pediatric hospital, which may limit the generalizability of our findings. Another limitation is that it is possible that a certain subset of patients with EFI had self-resolving symptoms and were therefore seen through routine gastroenterology or otolaryngology outpatient visits. This study did not identify patients who were managed exclusively as outpatients. An additional limiting factor is that not all patients who had EFI had a biopsy conducted. Of the 30 of 35 patients who had a biopsy conducted, 26 (87%) were diagnosed with EoE. Despite this limitation, our study has one of the highest biopsy rates (83%) compared to similar EFI studies; this high biopsy
rate represents a major strength of our analysis. In particular, a recent study by Hudson et al examined all patients with esophageal foreign body impactions to identify those with an underlying diagnosis of EoE. Similar to our study, the researchers found a high correlation between patients with EFI and EoE. However, it is important to note that the biopsy rate among their EFI cohort was only 51%. The fact that nearly half of all patients with EFI were discharged without a diagnostic esophageal biopsy further underscores the heterogeneity in management of EFI. The findings of the current study are in line with several recent publications that assert the importance of obtaining esophageal biopsies in all pediatric patients who present with EFI.

Conclusion

Most esophageal food impactions in the pediatric population are associated with an underlying diagnosis of EoE and are often the initial manifestation of the disease. EoE must be considered in all pediatric patients with EFI. Esophageal biopsies should be strongly considered in these patients at the time of endoscopic management of the EFI.

Author Contributions

Abhinav R. Ettyreddy, data analysis, drafting, final approval, accountability for work; Jacquelyn R. Sink, data analysis, drafting, final approval, accountability for work; Matthew W. Georg, data analysis, drafting, final approval, accountability for work; Dennis J. Kitsko, data analysis, drafting, final approval, accountability for work; Jeffrey P. Simons, data analysis, drafting, final approval, accountability for work.

Disclosures

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