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Scintigraphic Evaluation of Gastroesophageal Reflux and Pulmonary Aspiration in Children

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Gastroesophageal reflux (GER) and pulmonary aspiration are encountered in children of all ages. Signs, symptoms, and complications vary from mild and transient to severe life-threatening conditions. This review will present relevant clinical information on these conditions as well as common diagnostic procedures. The role of scintigraphic techniques used in the evaluation of these conditions will be discussed in detail including protocols and performance in comparison to other diagnostic methods.
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Evaluation of GER

Definitions

GER is the passage of gastric contents into the esophagus. Regurgitation implies that refluxed gastric contents reached the oropharynx whether or not it was expelled from the mouth. Vomiting is defined as expulsion of gastric contents from the mouth and is typically a forceful action. GER is a common phenomenon occurring at all ages in healthy individuals especially in infants. Most GER episodes are brief and often asymptomatic. GER disease (GERD) occurs when repetitive reflux episodes produce symptoms and complications.[1] It is not well established why GER is asymptomatic in some children and produces clinical symptoms in others. The frequency and duration of GER, gastric acidity, gastric emptying, esophageal mucosal barrier, esophageal clearing mechanisms, airway hypersensitivity, and genetic predisposition have been suggested as contributing factors in the pathogenesis of GERD.[2]

Prevalence and Clinical Presentations

Signs and symptoms of GERD are nonspecific, especially in the younger ages. Diagnostic tests are not routinely employed or indicated in all cases. Consequently, the prevalence of GER and GERD are hard to establish. GER is very common in healthy, well thriving infants. Some of these episodes result in regurgitation into the mouth. It is thought that transient relaxations of the lower esophageal sphincter, unrelated to swallowing, and inadequate adaptation of the sphincter tone to changes in abdominal pressure are the main mechanisms causing GER.[3,4] As the lower esophageal sphincter mechanism matures, the frequency of GER and regurgitation declines, and it is uncommonly seen beyond 18 months of age.[5-7] A study in healthy infants showed that at least one episode of regurgitation was encountered in 50% of 0-3 months old infants, peaking at 61% around the age of 4 months and declining to 21% between 6 and 7 months.[7] Symptoms attributed to GER were found in 1.8%-8.2% of children and in 3%-5% of adolescents.[6] Most regurgitation episodes are benign. One study, however, on a large cohort of infants found that frequent regurgitation during infancy increases the likelihood of developing GERD later in childhood.[8] Higher rates of GERD are encountered in preterm infants, children with severe neurodisabilities, children with cystic fibrosis, Down syndrome, repair of esophageal atresia, hiatal hernia, increased intra-abdominal pressure (abdominal mass and peritoneal dialysis), and in obese children.[9-12] An association exists between GERD and delayed gastric emptying. It has been shown in adults[13] but is less conclusive in children.[14-17]

Clinical manifestations and complications of GERD are encountered in the gastrointestinal (GI) and respiratory systems and vary with age. In infants, GERD often manifests as recurrent vomiting.[6,12] Distinction from "physiologic reflux and regurgitation" in healthy thriving babies may be difficult. A small percentage of infants present with complications of esophagitis including dysphagia, feeding difficulties, irritability, anemia, hematemesis, and failure to thrive. Respiratory complications may include wheezing, recurrent pneumonia,

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and rarely, bradycardia, apnea, and apparent life-threatening events. The causative relationship of reflux to these later complication is not clearly established.[1] Preschool children may present with recurrent episodes of regurgitation. Food aversion, poor weight gain, and wheezing may also be encountered but are insufficient symptoms for a definite diagnosis of GERD. GER is associated with asthma, possibly due to a reflex mechanism triggered by acidity in the esophagus resulting in bronchoconstriction.[18] Aspiration pneumonia is mainly encountered in neurologically debilitated children. In the rare Sandifer syndrome, GER is thought to trigger abnormal posturing consisting of back arching, torsion of the neck, and lifting of the chin mimicking a convulsive disorder.[9] The most common symptom in school-aged children and adolescents is chronic heartburn or regurgitation or both.[19] Some present with nausea, dysphagia, and epigastric pain. Esophageal strictures and Barrett esophagus[20] are encountered in some cases. Some children experience hoarseness due to reflux-induced laryngitis, and others may suffer from chronic cough and dental disease.[21] Sinusitis, asthma, recurrent pneumonia, and bronchiectasis can be additional manifestations of GERD in this age group.[22] Certain symptoms should raise the possibility of an alternative diagnosis or a serious coexisting disorder. These "red flags," listed in the National Institute for Health and Care Excellence (NICE) guidelines for the management of GER in children,[23] may suggest a different or accelerated diagnostic approach. Some of these symptoms include projectile vomiting, bilious vomiting (suggesting GI obstruction), hematemesis, bloody stools, diarrhea, abdominal distention, and neurologic deficiencies. Prominent systemic symptoms raise the possibility of infectious or metabolic conditions.

Diagnosis

Various diagnostic tests are available, but none can be considered as a gold standard. Some can demonstrate the presence of GER, and others may detect the consequences of GER. No test can adequately differentiate between "physiologic" and pathologic reflux.

Detailed history by itself is usually insufficient to distinguish between GERD and other conditions with similar presentations especially in infants (eg, infantile colic, cow's milk protein allergy).[24] Empiric treatment with proton pump inhibitors (PPIs) has been shown to be a cost-effective diagnostic technique in adults and may be useful in adolescents with uncomplicated heartburn.[9] This approach was not found to be effective for the diagnosis of GERD in infants and children. In a study of infants, with history suggestive of GERD, the therapeutic response to PPI and placebo trials were similar.[24]

Barium Contrast Radiography

Barium upper GI series were commonly employed in the past for the diagnosis of reflux. Nowadays, this study is considered inadequate for this purpose[12] with a lower sensitivity and specificity compared to esophageal pH studies.[25-27] The study may be difficult to perform in young, uncooperative children (who often refuse to drink the contrast). The observation period with videofluoroscopy is short in order to avoid excessive radiation exposure. Nevertheless, the anatomical details provided by barium swallow studies can be beneficial when other conditions in the differential diagnosis are suspected such as bowel malrotation, annular pancreas, and antral web.[27] When dysphagia is the predominant symptom, these studies can demonstrate esophageal strictures, achalasia, as well as hiatal hernia.

Endoscopy With Biopsies

Endoscopy can determine the presence and severity of esophagitis and complications, such as strictures or Barrett esophagus. The procedure can exclude other disorders such as eosinophilic, peptic, or infectious esophagitis.

Endoscopy allows visualization of damage to esophageal mucosa from acid reflux and associated complications. Biopsies increase the sensitivity of the test and help identify other conditions in the differential diagnosis such as eosinophilic esophagitis, allergic gastritis, and inflammatory bowel disease.[12] Endoscopy will not be helpful in cases of nonerosive GERD.[12] It is an invasive test requiring anesthesia but nevertheless, considered safe in infants and children. Complications and serious side effects are uncommon.[28]

Esophageal pH Monitoring and Impedance Monitoring

Prolonged esophageal pH monitoring requires placement of a transnasal catheter with a pH-sensitive probe in the distal esophagus. The esophageal pH is continuously monitored over 24 hours (the normal esophageal pH varies from 5-7). Drops in the pH below 4 indicate acid exposure suggestive of GER. The most important parameter provided by pH monitoring is the "reflux index." This index, defined as the percentage of time that the esophageal pH is less than 4, is an estimate of the cumulative esophageal acid exposure. The index, however, correlates weakly with clinical symptoms, presence of esophageal disease, and response to therapy.[1,9] An additional shortcoming of this test is its inherent disability to detect nonacidic reflux episodes. During the postprandial period, neutralization of gastric acidity of varying duration occurs and is affected by the patient's age, volume and composition of the meal, and the frequency of feeding. GER episodes during this period will not be detected by the pH monitoring.[29] It has been shown in infants and children that reflux-associated disturbances such as bronchitis, irritability, sleep disorders, episodes of apnea, oxygen desaturation, and pulmonary aspiration can be induced by both acidic ($pH < 4$) and nonacidic ($pH > 4$) reflux.[30] Multichannel intraluminal impedance (MII) monitoring provides measurements of bolus transit in the esophagus by detecting changes in electrical impedance during the passage of the bolus. This technique allows detection of both acidic and nonacidic reflux. It is common to combine this technique with pH monitoring by placing both pH and impedance probes on the transnasal catheter. In one study, combined pH-MII monitoring detected twice as many symptomatic reflux episodes as compared to pH monitoring alone.[31] Extended pH monitoring and MII, separately or combined, are invasive procedures requiring hospitalization