

A Case Report of a Young Patient with Dysphagia: Eosinophilic Esophagitis, Achalasia or Atypical course of Gastroesophageal Reflux Disease ?

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ABSTRACT

A 19 years old female patient presented with symptoms of dysphagia, esophageal retention and radiologic and endoscopic suspicion of esophageal stricture and achalasia in one other institution.

After extensive diagnostic procedure including upper gastrointestinal endoscopy with narrow-band imaging and histology of esophageal mucosa, Magnetic resonance imaging (MRI) of the thorax and abdomen, the 24h esophageal impedance pH monitoring and esophageal high-resolution monitoring. We have excluded eosinophilic esophagitis and achalasia, indicating to the atypical course of gastroesophageal reflux disease. The patient underwent the intense and combined pharmacologic (PPIs, H2 blockers, antacids) and endoscopic (repeated balloon-dilatation of esophagogastric junction stricture) therapy, over a period of two years. With this combined and long-lasting therapy, the patient significantly improved, clinically. The esophageal peristaltic activity was also recovered, thus incompletely. The patient remained well and gaining weight with minimal symptoms of dysphagia to solids, occasionally.

In presented case of a young female patient, we witnessed the overlapping nature of different criteria denoting the distinct entities, linked to esophageal dysphagia and esophageal motility disorder, such as achalasia, eosinophilic esophagitis and gastroesophageal reflux disease. The complex diagnostic approach, including esophageal functional testing pointed to the presence of gastroesophageal reflux disease, as to underlying condition for this complex clinical situation. The combined therapeutic approach, including antisecretory agents and repeated balloon dilatations led to significant clinical improvement.

Keywords

GERD, Esophageal monitoring, Esophageal manometry, 24-h impedance pH metry, GERD therapy.

Abbreviations

GERD: Gastroesophageal reflux disease, MRI: Magnetic resonance imaging, EoE: eosinophilic esophagitis, POEM: peroral endoscopic myotomy, narrow-band imaging (NBI), esophago gastric junction (EJG), distal contractility integral (DCI),

integrated relaxation pressure (IRP), lower esophageal sphincter pressure (LES).

Introduction

The presence of unremitting dysphagia, characterized with slow progression (months to years) is indicative of achalasia and bolus impaction is the characteristic of eosinophilic esophagitis (EoE) of longer duration. The long lasting esophagitis in gastroesophageal reflux disease (GERD) also represents the potential underlying

condition for development of dysphagia and esophageal obstruction, due to peptic stricture and/or esophageal cancer which is clinically linked to rapidly progressive, constant dysphagia [1-2]. However, The differential diagnosis of esophageal symptoms, especially dysphagia with suspicion of esophageal obstruction in young patients may represent a challenge to clinical practice [3-7].

Case Presentation

A 19 years old female patient presented with symptoms of dysphagia, esophageal retention and endoscopic suspicion of esophageal stricture. This initial evaluation was performed in another institution and the patient was advised to undergo peroral endoscopic myotomy (POEM), because of the diagnosis of achalasia. Due to a long-lasting symptoms, loss of weight and anxiety, and facing the complex endoscopic procedure, the young patient and her family decided to seek the second evaluation and opinion in our institution. The control evaluation in our institution included upper gastrointestinal endoscopy (Olympus Evis Exera III) in white and narrow-band imaging (NBI) and histology of esophageal mucosa, barium swallow, MRI of the thorax and abdomen, the 24h esophageal impedance pH monitoring and esophageal high-resolution monitoring, as well. The results of diagnostic work-up excluded the presence of eosinophilic oesophagitis and achalasia, indicating to the atypical course of gastroesophageal reflux disease (on barium swallow noted cicatrization and on MRI cicatrization was confirmed (Figure 1-A with white arrow) and revealed the absence of wall thickening and the level of esophago gastric junction (EGJ) (Figure 1-B with white arrow), on histopathology less than 15 eosinophils counted per high-power-field and mixed intraepithelial infiltrate that also included scarce eosinophils and PAS positive hyphae and spores indicative for candidiasis). Applying the minimal force, the passage of gastroscope to the stomach was possible during repeated endoscopies and the appearance of the gastric mucosa was normal, with negative *H. pylori* status on histology. The functional testing included the standard Laborie Medical measurement system MMS Solar-HRM 360° esophageal manometry with 36 channel water perfused catheter (according to Chicago 3 protocol with software for Chicago 3 and for mathematical adaptation of water perfused catheter to solid state catheters values) and with the standard procedure of 24h impedance pH-metry by using MMS pH metry system with 6 impedance and 2 pH metry sensors (analyzed according to Lyon consensus) [9-14].

The results of diagnostic work-up excluded the presence of eosinophilic oesophagitis and achalasia, indicating to the atypical course of gastroesophageal reflux disease.

According to standard Chicago 3 protocol [9-11], the esophageal manometry confirmed absent contractility with distal contractility integral (DCI) of 0 mmHg.s.cm (normal 450-8000 mmHg.s.cm), and without any pressurisation. The lower oesophageal sphincter pressure (LES) was 7mmHg (normal ≥ 10 mmHg) and integrated relaxation pressure (IRP) was 7 mmHg (<15mmHg) so the relaxation was not achieved, at all (Figure 1-C).

On standard procedure of 24h impedance pH-metry [12-14] we detected significant acid reflux (DeMeester score in the upper esophagus 169,37 and 226 in the lower esophagus, Key score up to 1040. Duration of reflux in the upper esophagus was 770 minutes and 918,9 minutes the the lower esophagus excluding postprandial time, with more than 401 impedance events (acid liquid and acid mixed- equal in upright and supine). During this 24h monitoring the patient did not register any symptom (Figure 1-D).

During the course of disease, after initial evaluation in our hospital, the patient experienced repeated episodes of aggravated dysphagia to liquids and solids and was treated with sessions of balloon dilatation (20 sessions over period of two years, 85-260 mm Hg/35-60 s, depending on local status of EGJ). The pharmacologic treatment started with the treatment of esophageal candidiasis, in combination with antisecretory therapy (full dose of 2 x 40 mg of pantoprazole daily, during 12 weeks; followed by combination of 40 mg of pantoprazole in the morning and 40 mg of famotidine in the evening).

The control manometries were performed at timepoint of 2 and 8 months after initiating the combined therapy with antisecretory drugs and repeated balloon dilatation of the EGJ. The first control manometry monitoring after 2 months documented the appearance of esophageal contractions, classified as ineffective contractions in 100% of swallows, and the second control monitoring after 8 months detected 10% of normal swallows, and 90% of ineffective swallows with minimum symptoms of esophageal retention. The (LES) arised to 10 mmHg, and IRP has lowered to 3,5 mmHg. The patient experienced the gradual improvement of the symptoms and control barium swallow documented the esophageal width od 2 cm with improved, but still somewhat slower pasasage of contrast media through EGJ to the stomach. On control endoscopy we have found no signs of esophageal inflammation with normal passage of the gastroscope to the stomach, without signs of retention in the esophagus. The histology of esophageal mucosa was also normal. The antisecretory therapy was continued and the regular controls were scheduled. The patient remained well and gaining weight with minimal symptoms of dysphagia to solids, occasionally.

The results of diagnostic work-up excluded the presence of eosinophilic oesophagitis and achalasia, indicating to the atypical course of gastroesophageal reflux disease.

The patient signed statement that informed consent was obtained from her for the purpose of publication. All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2013.

Discussion

We presented a case of a young female patient with symptoms of dysphagia, esophageal retention and inflammation, and incomplete obstruction at the level of EGJ. During six months, after clinically overt symptoms started, the course of the disease was characterized with occasional retrosternal pain, remittent alleviation of dysphagic

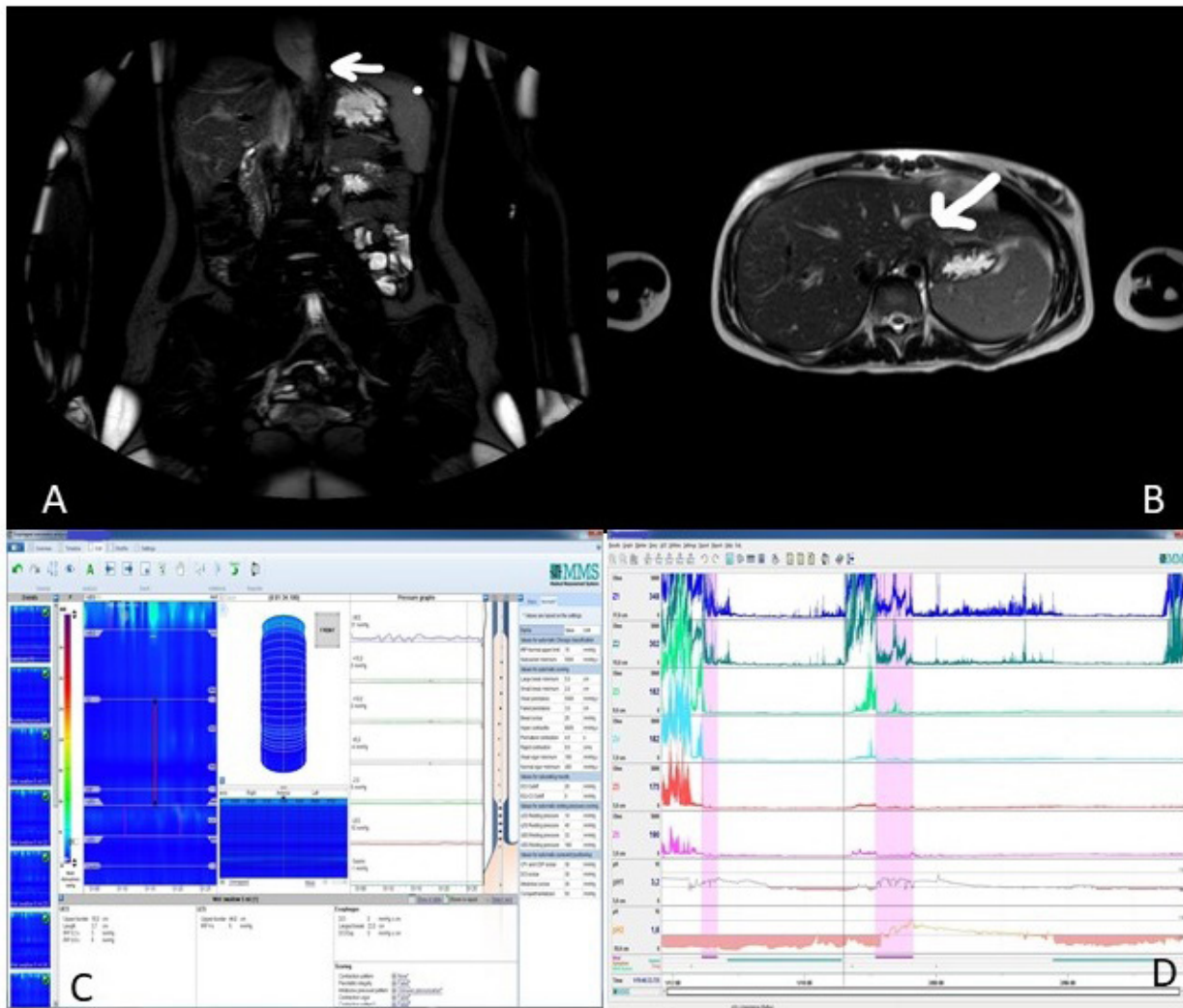


Figure 1. A) MRI image in axial projection with signs of esophageal dilatation and esophagogastric junction stenosis; B) MRI image in sagittal projection with no signs of esophageal muscular enlargement in lower esophagus; C) Esophageal manometry finding in one of ten swallows with absent peristaltic activity. The absent peristaltic activity is presented with blue colour on image (left) what represents low pressure and in the cumulative curves (on the right side); D) Results of 24h impedance pH measurement. The continuous acid reflux dominantly in lower esophagus and significant in the middle esophagus (lower two curves- the red color is attributed to pH < 4). The continuous impedance activity in esophagus (first six curves).

symptoms and cumulative progression of dysphagia to solids and liquids.

In teens and younger adults, the presence of gradually progressive and remittent dysphagia with esophageal motility alteration and obstructive symptoms may suggest the differential diagnosis between early achalasia, EoE and reflux disease of atypical course [3-7]. EoE represents immune-mediated (predominantly Th2-mediated), chronic and progressive disorder with clinical presentation in adolescents characterized by retrosternal and abdominal pain, dysphagia and food impaction as a typical and recurring symptom in older adolescents [15]. In addition, a published literature search on esophageal motility in eosinophilic esophagitis, using PubMed database identified the frequency of abnormal esophageal manometry between 4% and 86% in patients with EoE [16]. The authors of the mentioned literature search postulated that eosinophilic infiltration and remodelling of the

esophagus would be responsible of dysphagia and documented reduced distensibility, abnormal peristalsis and altered tonicity of the LES, which may also mimic other esophageal motility disorders, such as achalasia. Achalasia represents a primary esophageal motility disorder, characterized with absent peristalsis in the lower esophagus and incomplete lower esophageal sphincter relaxation, in response to swallowing (measured by IRP > 15 mm Hg) [17]. The novel 4.0 version of the Chicago Classification of primary esophageal motility disorders (PMED), based on high-resolution manometry added the term of „inconclusive diagnosis of achalasia“ with intention to decrease the unnecessary potential overtreatment of patients, especially with POEM [18]. In addition, a recent publication brought-up a retrospective analysis of prospectively collected data of 237 patients with achalasia, undergoing POEM, at a tertiary center (Prague, Czech Republic) [19]. According to the results of this study, about 20% of patients with achalasia, mostly of type II, have signs of partial recovery

of esophageal peristalsis, but the clinical relevance seems to be negligible.

It is important to emphasize that the manometric picture of gastroesophageal motility disorder can be due to GERD and it is mandatory to exclude abnormal reflux by pH monitoring, a notion which is known for many years [20].

A former approach which implied that EoE and GERD are mutually exclusive disorders has been overcome by observation that a certain number of patients, presenting with symptom typical of EoE and little evidence of GERD are responsive on PPI therapy, and the term PPI-responsive esophageal eosinophilia (PPI-REE) was created [21]. A consensus guidelines of A Working Group on PPI-REE (AGREE, 2018) considered PPIs, along with diet and topical corticosteroids as the established treatment for EoE [22].

Patients with GERD are not always presented with GERD symptoms and a certain number of patients do not have visible esophageal lesions on upper gastrointestinal endoscopy, especially the female patients that are more likely to have non erosive reflux disease (NERD) (5-7). The major problem in patients without symptoms and in the same time without esophageal lesions is to confirm the diagnosis of gastroesophageal reflux disease.

To clarify such a clinical situation, if the GERD is present or not in particular patient, esophageal function studies, high resolution manometry and 24h impedance pH-metry represent the gold standard of investigation. In this case, the female patient did not meet the full manometric criteria for achalasia and the 24h impedance pH-metry showed the pathologic acid reflux, as documented by DeMeester score, esophageal pH values, reflux duration and by impedance events.

We observed the absence of esophageal contractility, the LES pressure was too low for achalasia, without LES relaxation, as proven by the REST test. The persistence of the same pressure value during the resting period and on IRP test could speak in the favour of the hypothesis that the absence of relaxation would be due to fibrosis and not due to achalasia. Noteworthy, barium swallow noted the presence of esophageal mucosal cicatrization and histopathology of esophageal mucosa revealed the presence of mixed inflammatory infiltrate and esophageal candidiasis, in conjunction with incomplete obstruction, during initial evaluation and this condition was successfully treated with peroral and topical antimycotic agents. After combined therapy with antisecretory drug and balloon dilatation, the control evaluation showed the absence of overt mucosal inflammation and/or esophageal retention, and the passage of endoscope to the stomach was normal, without applying any force. The post-hoc argument for this therapeutic approach was the observation that the completely absent contractility at the beginning, recovered gradually after combined therapy protocol. The initial and control evaluation with 24h impedance pH-metry noted the pathologic acid reflux.

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Ethical Statement

The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee(s) and with the Helsinki Declaration (as revised in 2013). Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the editorial office of this journal.

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