Esophageal Inlet Patch: An Under-Recognized Cause of Symptoms in Children

Giovanni Di Nardo, MD, PhD[1,2], Cesare Cremon, MD[3], Luca Bertelli, MD, PhD[3], Salvatore Oliva, MD[4], Roberto De Giorgio, MD, PhD[3], and Nico Pagano, MD[3]

Objectives To determine the incidence of inlet patch (IP) and to assess the clinical and pathological features, role of the diagnostic workup in treatment decision making, efficacy of medical and endoscopic therapy, and natural history in a pediatric population.

Study design Consecutive patients aged <18 years (n = 1000) undergoing esophagogastroduodenoscopy were enrolled prospectively. Biopsy specimens were obtained from IPs and the proximal and distal esophagus, stomach, and duodenum. Multichannel intraluminal impedance and pH monitoring (MII-pH) was performed in all symptomatic patients. Symptomatic patients were treated with proton pump inhibitors for 8 weeks, and IP ablation by argon plasma coagulation (APC) was performed in unresponsive patients.

Results The endoscopic incidence of IP was 6.3%, with a cumulative missing rate of 5.8%. Thirty-five of the 63 patients (56%) were asymptomatic, 11 (17%) had symptoms clearly related to the underlying digestive disorder, and 17 (27%) had chronic IP-related symptoms. MII-pH was positive in 10 of the 28 symptomatic patients. All 17 patients with IP-related symptoms were unresponsive to proton pump inhibitors and were treated with APC, and all had achieved complete remission by the 3-year follow-up. Patients with underlying disorders were successfully treated with medical therapy, and asymptomatic patients remained symptom-free, with no endoscopic or histological changes seen at the 3-year follow-up.

Conclusion IP is an under-recognized cause of symptoms in children with unexplained esophageal and respiratory symptoms. MII-pH and bioptic sampling are needed to exclude entities mimicking IP symptoms and to direct therapy. APC is safe and effective for treating IP-related symptoms. *(J Pediatr 2016;176:99-104)*.

An inlet patch (IP) is a salmon-colored, velvet-appearing, distinct area of heterotopic gastric mucosa typically located in the proximal esophagus just distal to the upper esophageal sphincter. It is usually a single lesion but can be multiple, ranging in size from a few millimeters to >5 cm.[1-3]

The endoscopic-detected incidence of IP ranges from 0.1% and 10% in published studies.[1,4-6] The true incidence may be underestimated; in daily practice, IP is often missed during routine endoscopy. This might be related to the fact that the lower part of the esophagus is more often in the focus of the endoscopist, owing to the frequent pathological findings in this area.[5,7,8]

Although generally asymptomatic, the presence of IP has been associated with laryngopharyngeal symptoms (ie dysphagia, laryngospasms, hoarseness, globus throat discomfort, and chronic cough), likely related to acid production.[4,9-13] IPs also have been linked to complications including esophageal strictures, tracheoesophageal fistula, ulcerations, bleeding, and perforation.[14-18] Furthermore, in an autopsy study of a pediatric population, the presence of an IP was associated with unexplained death; the authors speculated that pulmonary aspiration of esophageal contents may cause death in some of these children.[19]

IPs are also potential sites for *Helicobacter pylori* infection.[18,20] In addition, Barrett esophagus and adenocarcinoma within IPs have been reported in adults, proving its potential, albeit rare, malignant progression.[21-32]

To date, only a few studies on IP in the pediatric population have been published, most of which are in case report form and limited by their small sample size and retrospective design.[10,11,33-38] The aims of the present prospective study were to assess: (1) IP in a pediatric population in which the endoscopist is sensitized to search for this entity; (2) the associated clinicopathological

APC	Argon plasma coagulation
AR	Acid reflux
EGD	Esophagogastroduodenoscopy
EoE	Eosinophilic esophagitis
GERD	Gastroesophageal reflux disease
IP	Inlet patch
MII-pH	Multichannel intraluminal impedance and pH monitoring
PPI	Proton pump inhibitor
RSI	Reflux symptom index
SAP	Symptom association probability
SI	Symptom index

From the [1]Pediatric Unit, Orvieto Hospital, Orvieto, Italy; [2]Pediatric Gastroenterology Unit, International Hospital Salvator Mundi, Rome, Italy; [3]Department of Medical and Surgical Sciences, University of Bologna, St Orsola-Malpighi Hospital, Bologna, Italy; and [4]Pediatric Gastroenterology and Liver Unit, Department of Pediatrics, Sapienza University of Rome, Rome, Italy.

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features of IP; (3) the role of the diagnostic workup in treatment decision making; (4) the efficacy of medical and endoscopic therapy; and (5) the natural history of IP.

Methods

Consecutive patients aged <18 years (n = 1000; 621 females) undergoing esophagogastroduodenoscopy (EGD) for various indications were prospectively assessed for the presence of IP between January 2011 and December 2012 at the Pediatric Gastroenterology Units of the University of Rome and University of Bologna. Patients who underwent endoscopy for such indications as urgent, interventional, capsule placement, enteroscopy, and systemic disorders (eg, Sjögren syndrome, scleroderma) were excluded. The appropriate Institutional Ethical Committees approved the study design. Written informed consent was obtained from all parents, and children when applicable, after they received a thorough explanation of the research protocol.

Before EGD, all patients were carefully questioned about symptoms experienced within the previous month using a self-administered 9-item reflux symptom index (RSI).[39] Patients graded the severity of each item from 0 (none) to 5 (severe problem). Clinical response was defined as a reduction in clinical score of at least 3 points for each symptom.

Endoscopic Procedures

All EGD procedures were performed under general anesthesia by an experienced endoscopist using a video gastroscope (GIF-180; Olympus, Hamburg, Germany). During the procedure, the esophagus was carefully surveyed, with particular attention to the area of the upper esophageal sphincter. This area was best examined by slowly withdrawing the endoscope, with repeated short inflations while rotating the instrument.

IPs were identified as patches covered with salmon-red mucosa distinguishable from surrounding grayish-pearl–colored esophageal mucosa by well-defined margins (**Figure 1**, A). Each IP was measured by comparing it with the length of the metallic tip of the biopsy forceps (5 mm). In patients with multiple patches, the sizes of all patches were summed. Reflux esophagitis and Barrett esophagus were surveyed and classified according to the Los Angeles classification system[40] and the Praque C & M criteria,[41] respectively. Hiatal hernia was considered when the maximum length of the gastric mucosal folds above the gastroesophageal junction exceeded 20 mm.

Histopathological Assessment

At least 2 biopsy specimens were obtained from each IP using disposable endoscopy biopsy forceps (EndoJaw FB 230V; Olympus). Biopsy specimens were also obtained from the proximal and distal esophagus, fundus, antrum, corpus, and duodenum of the patients with an IP. All biopsy specimens were blindly reviewed by a single pathologist. The squamous mucosa was examined for changes of reflux esophagitis,[42] and the columnar mucosa was examined for the presence and degree of inflammation and/or intestinal metaplasia according to the modified Sydney classification system.[43] IP mucosal type was classified based on the presence of parietal and chief cells as antral type, fundic type, or transitional type. The presence of *H pylori* was evaluated using hematoxylin and eosin and Giemsa staining in the IP and the gastric mucosa.

Multichannel Intraluminal Impedance and pH Monitoring

The presence of gastroesophageal reflux or IP-related acid production was assessed using multichannel intraluminal impedance and pH monitoring (MII-pH). For ethical reasons, MII-pH was performed only in symptomatic patients with IP.

The procedure was performed with a combined MII-pH flexible catheter (Covidien-Medtronic, Minneapolis, Minnesota) with 8 impedance rings (representing 6 impedance channels) and 2 antimony pH sensors. The distal pH sensor was located at 4.5 cm from the catheter tip, and the proximal pH sensor was located 15 cm from the distal sensor. The 6 impedance channels were located in the MII-pH probe at -2, 0, 2, 4, 13, and 15 cm from the distal pH sensor. The probe was then

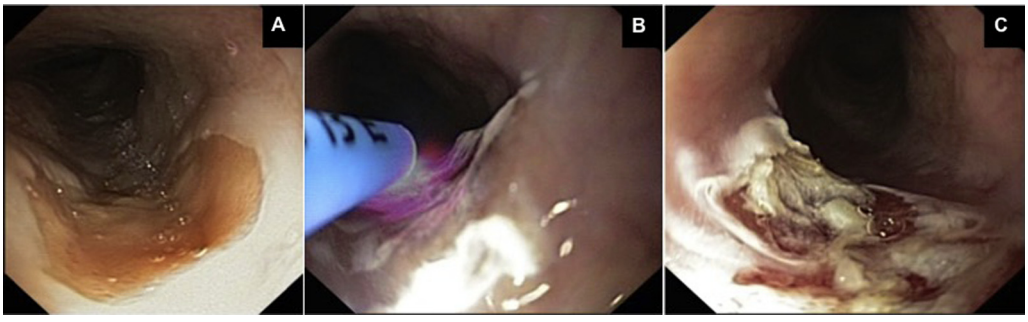

Figure 1. **A,** Typical endoscopic appearance of IP. **B,** IP treatment with APC. **C,** Endoscopic findings at the end of the APC treatment.