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The First Reported Case of Peroral Endoscopic Myotomy in a Child in Portugal

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Keywords
Allgrove syndrome · Achalasia · Peroral endoscopic myotomy

Abstract

Introduction: Achalasia is a rare disorder, with few cases occurring during childhood. It is also part of the Allgrove syndrome phenotype and a clinical feature that has a major impact on children's development. Timely diagnosis and effective treatment of symptoms are essential. The novel peroral endoscopic myotomy (POEM) may represent an effective alternative in children. ***Case Presentation:*** We present the case of a female child born in 2013, without relevant family history or perinatal events. At 6 years old, she presented with seizures related to recurrent hypoglycemia episodes, and adrenal insufficiency was diagnosed. Two years later, the patient was referred to our institution due to regurgitation and vomiting, causing failure to thrive. After an upper endoscopy with no significant findings, high-resolution manometry revealed type II achalasia. Alacrima was also part of the clinical picture, and Allgrove syndrome was genetically confirmed. Due to significant symptoms, an endoscopic pneumatic dilation was performed, with transient relief of symptoms. After a second pneumatic dilation and several hospitalizations due to achalasia complications, a POEM was considered. She underwent POEM in March 2024, without adverse events and excellent short-term outcomes. ***Discussion:*** Although there is limited literature on POEM in children, the results demonstrate an encouraging success rate, compared to pneumatic dilation and laparoscopic Heller's myotomy. We present the first reported case of POEM performed in a child in Portugal. The long-term efficacy of this promising minimally invasive procedure should be assessed in the pediatric population.

O primeiro caso reportado de miotomia peroral endoscópica numa criança em Portugal

Palavras Chave
Síndro de allgrove · Acalásia · POEM

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Resumo

Introdução: A acalásia é uma doença rara, com poucos casos descritos durante a infância. A acalásia faz parte da síndrome de Allgrove e é uma entidade com grande impacto no desenvolvimento infantil. O diagnóstico atempado e a terapêutica efetiva dos sintomas são essenciais. A emergente miotomia *peroral* endoscópica (POEM), poderá representar uma alternativa em idade pediátrica. ***Caso Clínico:*** Apresentamos o caso de uma criança do sexo feminino nascida em 2013, sem antecedentes familiares ou eventos perinatais de relevo. Aos seis anos, por apresentar convulsões associadas a episódios recorrentes de hipoglicemia, foi diagnosticada com insuficiência suprarrenal. Dois anos depois, foi referenciada à nossa instituição por regurgitação e vómitos com impacto na progressão estaturo-ponderal. Após uma endoscopia digestiva alta considerada sem alterações, a manometria de alta-resolução revelou critérios de acalásia tipo II. Verificou-se também a existência de alacrimia e a síndrome de Allgrove foi confirmada por teste genético. Atendendo aos sintomas, foi realizada endoscopia com dilatação pneumática, com alívio temporário de sintomas. Após uma segunda dilatação pneumática e vários internamentos por complicações de acalásia foi considerada a realização da POEM. A doente foi submetida à POEM em março de 2024, sem eventos adversos e com excelentes resultados no período de seguimento a curto prazo. ***Discussão:*** Embora existam dados limitados em relação à POEM na população pediátrica, os resultados são encorajadores, comparando com a dilatação pneumática e miotomia de Heller laparoscópica. Apresentamos o primeiro caso reportado de POEM realizado numa criança em Portugal. São necessários mais dados sobre a eficácia a longo prazo deste procedimento minimamente invasivo na população pediátrica.

Introduction

Achalasia is a rare disorder with an incidence of 1.6 cases per 100,000, affecting males and females equally [1]. The disease can occur at any age, but onset before adolescence is rare with less than 5% of cases diagnosed under 15 years of age [1, 2]. It is characterized by esophageal dysmotility and lack or incomplete relaxation of the lower esophageal sphincter (LES). According to high-resolution manometry, achalasia is classified into 3 types [3], with type II being the most common. Type II achalasia is characterized by abnormal median integrated relaxation pressure and absent contractility, with all failed swallows and at least 20% of swallows with panesophageal pressurization [3]. The 12-point Eckardt score assesses clinical severity of achalasia, regarding dysphagia, regurgitation, retrosternal pain, and weight loss. Achalasia may occur in association with adrenocorticotropic hormone-resistant adrenal insufficiency and absent lacrimation in patients with Allgrove syndrome, a rare autosomal recessive genetic disorder [4].

In the pediatric population, achalasia impacts development and quality of life, requiring effective therapy for successful child development. Nifedipine, botulin toxin injection, pneumatic dilation, and Heller's myotomy represent diverse therapeutic options [5]. However, there are few comparative studies and a heterogeneity of methods applying the existing therapeutic options in the pediatric population. New therapeutic methods, such as peroral endoscopic myotomy (POEM), are yet to be included in this therapeutic algorithm [5]. We present the first reported case of POEM performed in a 10-year-old child in Portugal.

Case Report

We present the case of a female child born in 2013 with no consanguinity or relevant family history. Pregnancy was uneventful and was followed by a full-term birth. There were no issues during birth or neonatal period. The patient was exclusively breastfed for the first 6 months, and complementary feeding was successful, promoting adequate nutritional status as well as physical and psychological development. There were no pathological regurgitation events. Since the age of 4, she was considered a picky eater and started to reject some foods from the family's usual menu and preferred baby food.

In 2019, at the age of 6, multiple seizure episodes related to recurrent hypoglycemia ultimately led to the diagnosis of primary adrenal insufficiency. The patient started hydrocortisone daily, with good clinical response.

At 8 years of age, due to failure to thrive following frequent vomiting, she was referred to Pediatric Gastroenterology in our institution for investigation. At that time, the patient's weight percentile dropped from between the 25th and 50th percentile to below the 5th percentile, while the height percentile dropped from between the 10th and 25th percentile to below the 5th percentile.

After an upper endoscopy with biopsies which revealed no significant endoscopic or histologic findings, an esophageal X-ray with contrast showed a persistently narrowed region at the end of the esophagus with a dilated esophagus above the narrowed region (Fig. 1). Hereafter, high-resolution manometry revealed type II

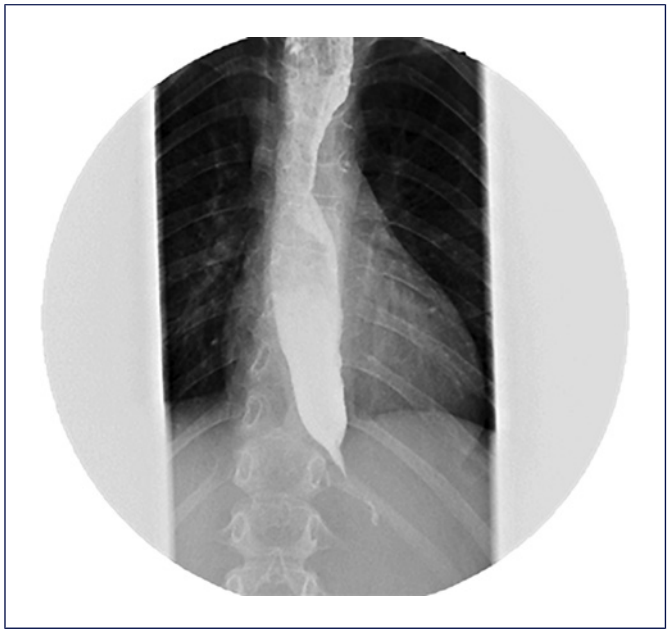

Fig. 1. Esophageal X-ray with contrast showing a persistently narrowed region at the end of the esophagus with a dilated esophagus above the narrowed region.

achalasia, characterized by residual LES relaxation with an integrated relaxation pressure of 55.0 mm Hg (normal: less than 15.0 mm Hg) and 100% of failed swallows with 80% of panesophageal pressurization (Fig. 2).

Upon further evaluation, it was noted that the patient had been crying without tears since birth, a condition known as alacrima. Adding the already previously known diagnosis of adrenal insufficiency and the recent diagnosis of achalasia to the clinical picture, Allgrove syndrome was considered. It was then genetically confirmed in February 2022, as a mutation in the AAA (achalasia-addisonianism-alacrima) gene, which encodes the ALADIN protein.

In February 2022, the 8-year-old child was highly symptomatic, experiencing daily dysphagia, thoracic pain, regurgitation after every meal, and a significant 8% weight loss in 9 months. Despite the lack of validation for the pediatric population, the Eckardt score was applied and revealed a value of 9. Treatment of achalasia was urgent, and an endoscopic pneumatic dilatation was considered as an attempt to improve her clinical condition.

A pneumatic dilation was performed using a 30 mm diameter Rigiflex® balloon under fluoroscopic control. The balloon was inflated until the waist in the middle of the balloon was no longer visible, maintained for 60 s, and then deflated. There were no adverse events during the procedure.

Due to a transient improvement on symptoms after the first endoscopic procedure, a second pneumatic dilation was performed 6 months later, using again a 30 mm diameter Rigiflex® balloon. No adverse events during this procedure were reported.

However, over the following 12 months, the patient experienced progressive worsening of dysphagia and frequent nighttime cough, requiring three hospital admissions (November 2022, July 2023, and September 2023) due to regurgitation and inability to feed orally. Subsequent contrast esophagram showed reduced peristalsis, a 32 mm esophageal caliber with probable alimentary debris, and distal esophageal stenosis.

Due to worsening of symptoms, a multidisciplinary team including pediatric gastroenterologists, pediatric surgeons, and gastroenterologists proposed POEM intervention. At the time, the patient presented an Eckardt score of 10.

On March 2024, POEM was performed. Endoscopic evaluation of the mucosa revealed no particularities; after determination of the distance to the cardia, a submucosal injection with normal saline and indigo carmine was performed at 8 cm from gastroesophageal junction. An esophageal mucosal longitudinal incision was made with DualKnife J (1.5 mm), and a submucosal tunnel was created on the posterior esophageal wall extending 2-cm distal to the cardia. A complete 6-cm myotomy was performed, leading to no bounces on the gastroesophageal junction. The tunnel was closed with 7 through-the-scope clips (Fig. 3). The procedure had no adverse events.

The patient received antibiotic prophylaxis with intravenous ceftriaxone (50 mg/kg/day). Following a control esophagram 48-h after the procedure without contrast overflow and rapid esophageal clearance (Fig. 4), the patient started a liquid diet for 7 days, with good tolerance, and then progressed to a soft diet. Additionally omeprazole (1 mg/kg/day) was prescribed for gastroesophageal reflux prophylaxis.

At a follow-up appointment 6 weeks after the procedure, an Eckardt score of zero was registered. She had no dietary restrictions and reported no symptoms, including dysphagia, thoracic pain, or regurgitation, and a weight increment of 4.5 kg (19% of body weight) was noticed. The child resumed her daily life with family, friends, and school, showing potential for complete physical and psychological development.

The patient will continue to be monitored for symptoms and long-term outcomes at Pediatric Gastroenterology appointments. According to institutional protocol, impedance pH monitoring without proton pump inhibitor (PPI) therapy is performed 3 months after the procedure to evaluate gastroesophageal reflux

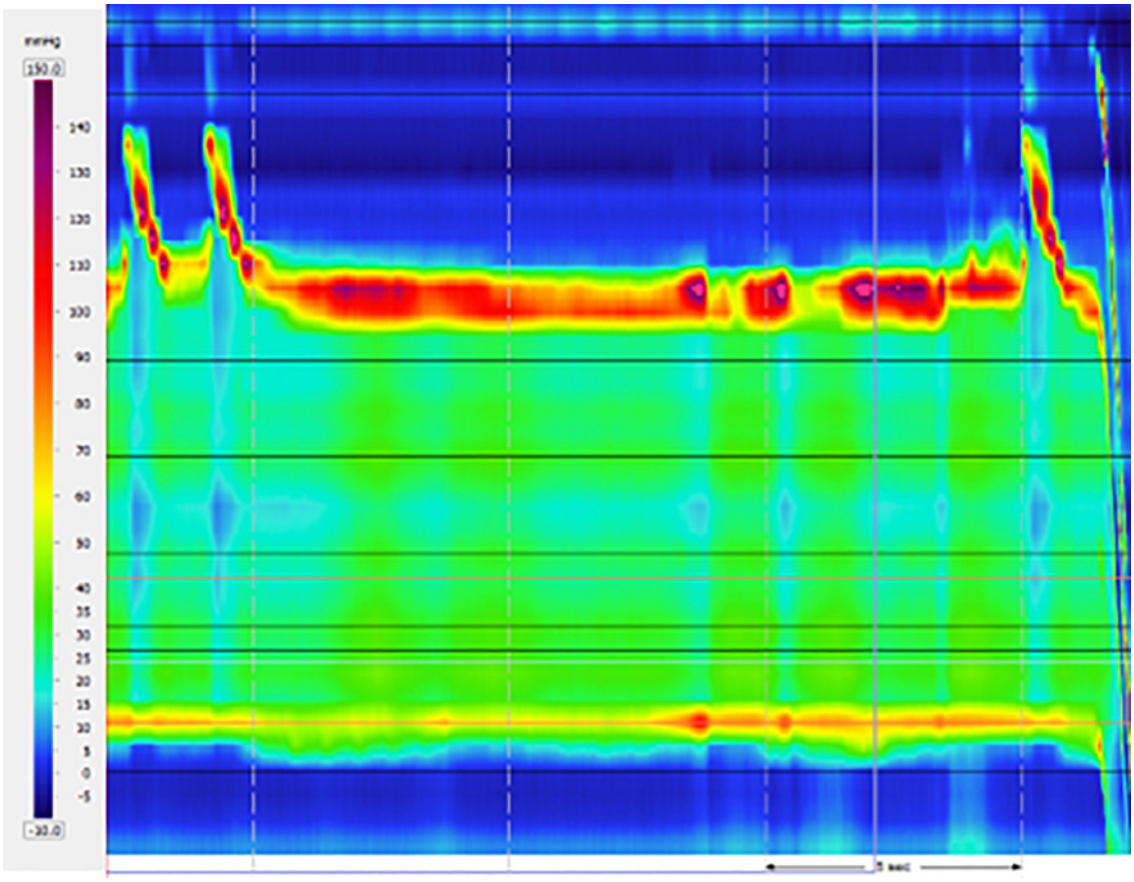

Fig. 2. High-resolution manometry consistent with type II achalasia.

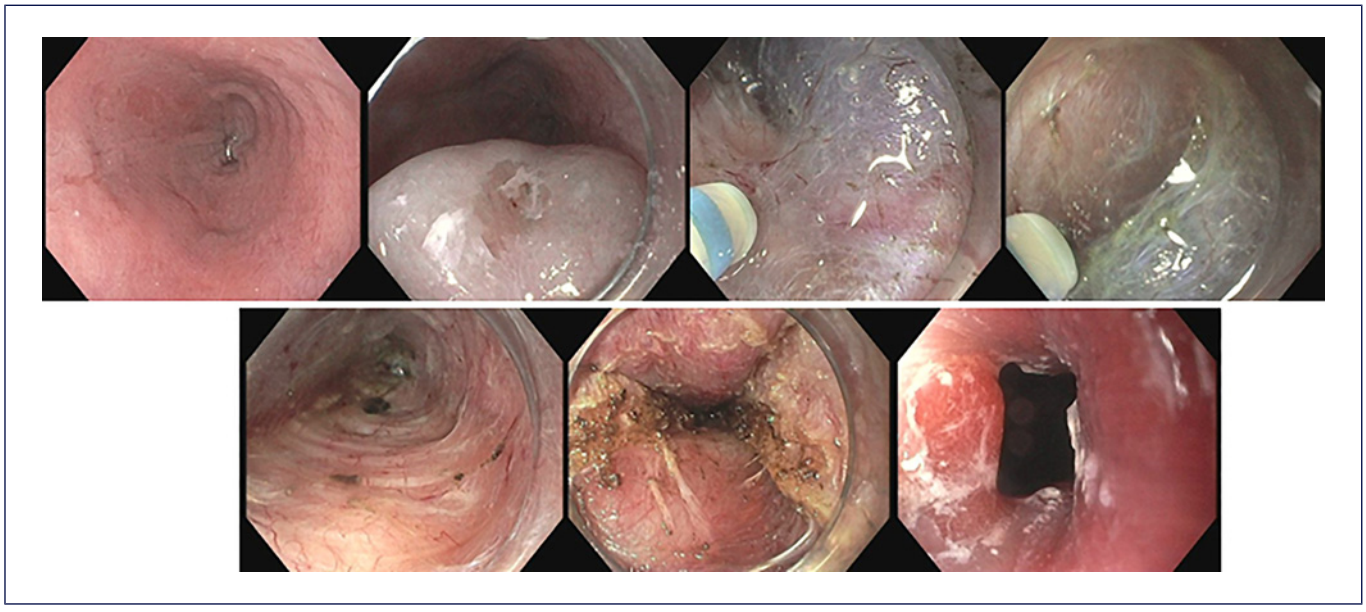

Fig. 3. POEM step-by-step in images.

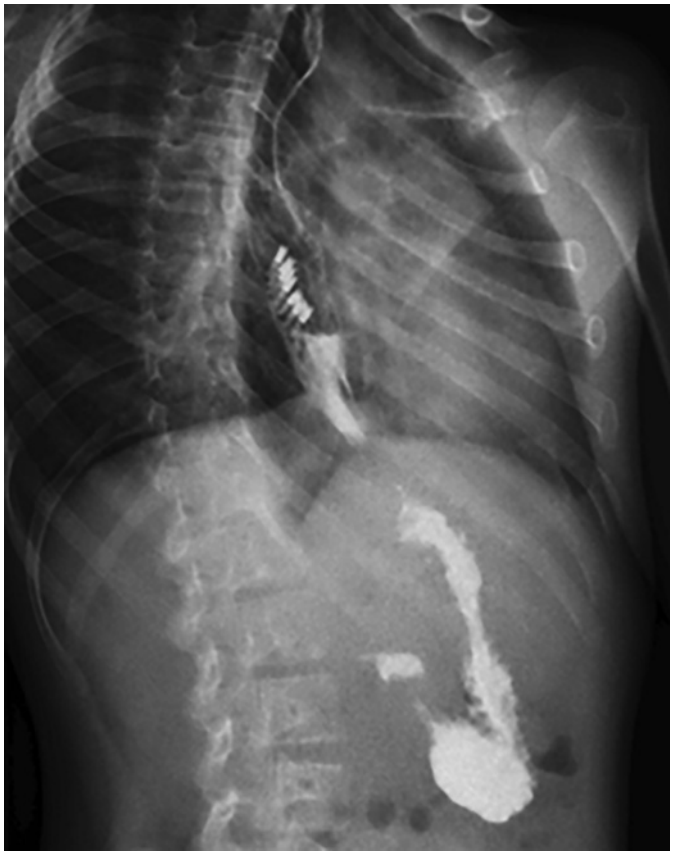

Fig. 4. Esophagram after POEM.

and determine whether to continue therapy. In this case, impedance pH monitoring was postponed to 6 months after the procedure due to family constraints, and she maintains omeprazole (1 mg/kg/day).

Discussion

Achalasia significantly impacts development and quality of life in the pediatric population due to dysphagia, thoracic pain, regurgitation, and weight loss. The goal of therapy is symptoms relieve, to ensure the successful children development and promoting reestablishment of quality of life.

The use of botulinum toxin is rare considering its short-term effectiveness in symptom relief (averaging about 4 months) and the long-term survival in pediatric achalasia cases [2]. In this population, it would imply to repeat a therapeutic endoscopy several times a year (with permanent relief in 10%–40% of adult cases) [2]. The literature provides insufficient evidence to determine whether pneumatic dilation or laparoscopic Heller's myotomy (LHM) is superior as a first-line treatment for pediatric achalasia [5].

Pneumatic dilation of the LES is considered an acceptable initial treatment for achalasia in children, as demonstrated in our clinical case [2]. Although a mean success rate of 44.9% on symptom improvement and weight gain was identified in the systematic review by Goneidy et al. [5], there is a variation in methods and success rates among several authors [6]. This may account for different therapeutic algorithms used across different institutions. Additionally, the initial response to treatment can predict the success or failure of subsequent dilatations [2]. In our case, due to a transient improvement on symptoms, we repeated pneumatic dilation of the LES. However, multiple dilations are often required to achieve successful symptom relief and long-term results are inferior to LHM [6].

POEM is an endoscopic procedure highly effective in treating adult patients with achalasia. In a meta-analysis, the improvement in dysphagia at 12 months was 93.5% for POEM and 91.0% for LHM ($p = 0.01$), and at 24 months, it was 92.7% for POEM and 90.0% for LHM ($p = 0.01$) [7]. Furthermore, patients who underwent POEM had fewer short-term complications related to the procedure (less than 5%). However, those undergoing POEM were more likely to develop gastroesophageal reflux disease (GERD) (symptomatic, erosive esophagitis, or by pH monitoring, all $p < 0.0001$) [7].

The first reported cases of POEM performed in children date back to 2012 [8]. A recent meta-analysis evidenced a success rate of 99.3% for POEM compared to 77.9% for LHM [5]. In a meta-analysis, on short-term follow-up (less than 12 months), POEM was associated with a significant mean reduction in Eckardt score by 6.36 points (4.93–7.78, $p < 0.001$) and a reduction in LES pressure of 19.26 mm Hg (16.58–21.94, $p < 0.001$) [9].

Although there were more adverse events (24.4%) described in children compared to adults, these were mainly GERD and mucosal tears with no clinical significance (9.7%) [5]. The incidence of clinically significant adverse events, such as perforations (3 in 187 cases), was very rare, with only 0.01% requiring surgical intervention [5].

There are few reports on long-term outcomes of POEM in pediatric patients. A meta-analysis by Lee et al. [9] identified a significant mean reduction in Eckardt score by 6.88 points (6.28–7.48, $p < 0.001$) and in LES pressure of 20.73 mm Hg (15.76–25.70, $p < 0.001$) with long-term follow-up (more than 12 months). More recently, Bi et al. [10] published a series of 37 cases with a mean follow-up of 5.7 years, with promising results in reducing Eckardt score (8.0 [4–11] vs 1.1 [0–4], $p < 0.001$). They also reported improvements in subscores for dysphagia (2.8 ± 0.7 vs

0.6 ± 0.7, $p < 0.001$), regurgitation (1.7 ± 0.8 vs 0.1 ± 0.2, $p < 0.001$), chest pain (1.0 ± 0.9 vs [0.4 ± 0.6, $p < 0.001$] and weight loss [1.5 ± 1.2 vs 0.0 ± 0.0, $p < 0.001$]). Additionally, the study assessed the number of months of school absence, which decreased from a mean of 3.3 (0.5–24) months pre-POEM to 0.1 (0–1) months post-POEM [10]. Finally, the advantages of a minimally invasive procedure such as POEM as compared to the requirements of a surgical procedure should also be emphasized.

Other authors that confirmed the clinical success of POEM in pediatric population also reported erosive esophagitis in endoscopy (57.1%) and gastroesophageal reflux symptoms (13.8%) with a mean 69 months of follow-up [11]. The reported cases of erosive esophagitis were mostly mild (grade A or B in the Los Angeles classification), and similar to the adult population, the majority of patients are asymptomatic for GERD [11].

Our institutional protocol includes a pH monitoring 3 months following the procedure, after PPI withdrawal. However, to our best knowledge, there is no literature on adequate time for PPI treatment or validated systematic approach for managing GERD post-POEM, considering both short- and long-term complications. There is also a lack of data on which percentage of children are unresponsive to PPI and subsequent therapeutic options. Considering children with GERD, there were no relevant adverse events when PPI treated comparing to placebo, and antireflux surgery is the only procedure considered for refractory GERD due to lack of data regarding endoscopic procedures [12]. This is a relevant topic considering the overall survival of children with achalasia after POEM.

Overall, available data enhance POEM as an effective and safe long-term treatment option in pediatric achalasia cases. However, its feasibility depends on the availability of highly trained endoscopic teams experienced in the POEM procedure. Although there are few centers performing POEM in Portugal, data are scarce regarding its numbers and experience using this technique, except for a prospective study for one reference center [13]. Establishing institutional reference centers could improve access to POEM, particularly for the pediatric population. Additionally, further research on the therapeutic outcomes of achalasia in pediatric cases would be pivotal, regarding long-term data on quality of life and impact on child development.

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Statement of Ethics

This type of manuscript, case report, does not require an ethical approval according to national laws. A written informed consent was obtained from parents for publication of the details of medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Inês Coelho Rodrigues: part of endoscopic team, preparation, creation and writing of draft, and revision of draft version. Luís Rodrigues: patient's assistant physician and revision of draft version. Miguel Moura: main endoscopist and revision of draft version. Ana I. Lopes and Luís Correia: revision of draft version.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

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