Congenital Esophageal Myofibrotic Stenosis as a Rare Cause of Progressive Vomiting and Faltering Growth in a 5 Month-old: A Case Report and Review of the Literature

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Keywords
Congenital oesophageal stenosis ; myofibrotic stenosis ; faltering growth ; non-bilious vomiting ; infant.

Abstract
Congenital oesophageal stenosis is a rare congenital anomaly of the gastro-intestinal tract characterized by a fixed narrowing of the oesophagus. Onset of symptoms such as vomiting, dysphagia and faltering growth is variable, depending on the extent of the stenosis. There is often a significant delay between first symptoms and diagnosis We report on a five month-old infant presenting with symptoms of progressive nonbilious vomiting and weight loss. The diagnosis in this case was revealed by upper gastro-intestinal endoscopy after failed attempts to place a nasogastric feeding tube.

Introduction

Vomiting accompanied by faltering growth is relatively common in young children attending daycare centres, usually due to repeated viral infections. However, when vomiting persists, it may indicate underlying conditions such as congenital anomalies, pyloric stenosis, malrotation or metabolic disorders (1,2).

Congenital oesophageal stenosis (CES) is a rare cause of non-bilious vomiting in infants. CES is a congenital condition characterized by an intrinsic, fixed narrowing of the oesophagus, with an estimated incidence of 1 in 25.000-50.000 live births (3). It can appear in isolation or alongside other congenital anomalies, which has been reported in 17-42% of the cases across different series (1,4,5). It is most frequently associated with oesophageal atresia (0.4-14% of CES patients), The largest published case series to date is a multicentre study involving 61 CES patients from the French network of Oesophageal Malformations and Congenital disease, of whom 48% were also diagnosed with oesophageal atresia (6). Examples of other associated anomalies are congenital heart disease, trisomy 21, other gastrointestinal anomalies (such as anorectal malformations and duodenal atresia), tracheomalacia and hiatal hernia (1,2,6,7,8,9).

Case

Patient presentation

Informed consent for this case report was given by both parents of our patient. A 5-month-old boy was referred to the emergency department with a one-week history of upper respiratory symptoms and mild respiratory distress for the past 24 hours. The parents also reported a month-long history of vomiting and weight loss, with worsening symptoms over the past week. The vomiting, which occurred immediately after feeding, was non-bilious. His intake had decreased by 50% compared to a month ago and he had lost 500 grams in 14 days. Despite the parents' attempts to introduce solid foods two weeks before presentation, the boy consistently refused them. The patients medical history included two prior admissions at two weeks and two months of age due to non-bilious vomiting and faltering growth, both followed by a period of catch-up growth (see Figure 1). His weight-for-age percentile dropped from the 25th to below the 3rd centile, and his length-for-age centile decreased from the 50th to the 25th centile (Figure 1). Clinical examination revealed no abnormalities. During observation at the emergency department, the child experienced two short episodes of apnoea with desaturation, prompting admission for further observation.

Laboratory investigations revealed mildly elevated inflammatory markers but no hypoglycaemia or electrolyte imbalances. An abdominal ultrasound showed no anomalies, including a normal pyloric diameter. The initial diagnosis was persistent vomiting due to viral infection. During hospitalization, no additional episodes of desaturation or apnoea were observed, but the child continued projectile vomiting multiple times a day and failed to gain weight.

Nasogastric tube placement attempted by the nursing staff and otorhinolaryngology team remained unsuccessful. An upper endoscopy was performed and revealed an oesophageal pinpoint stenosis at the level of the lower oesophageal sphincter, located 17 cm from the dental arch (Figure 2). Prestenotic dilatation of the oesophagus was also noted. During the procedure a balloon dilation up to 6cm H2O (corresponding to ±7mm diameter) was performed resulting in a residual lumen of 2-3 mm, which allowed

for the successful placement of a nasogastric feeding tube (ch 8). Histological examination of the stenotic area showed granulation tissue (Figure 3). Biopsies of the rest of the oesophagus did not show any changes compatible with reflux esophagitis or eosinophilic esophagitis. Imaging, including a contrast study of the upper gastro-intestinal tract, CT scan and MRI showed no evidence of tracheobronchial remnants.

Follow-up and outcomes

Following this diagnosis, a proton pomp inhibitor was started to facilitate healing of the tears after dilatation and feeding through the nasogastric tube was continued resulting in catch-up weight gain. In the eight first months after diagnosis, repetitive endoscopic balloon dilations were performed with intervals between dilatations varying from one to four weeks. Because of recurrent restenosis, intralesional injection with triamcinolone was performed the first time at four months after diagnosis. This treatment was repeated four times over a period of four months with less pronounced restenosis between dilatations. No more dilatations were needed in the four months since the last Triamcinolone injection with repeat endoscopies showing a persistent lumen allowing passage of an adult endoscope, corresponding with 9.9 mm diameter. Tube feeding could be stopped at 4 months after diagnosis.

Discussion

We report a rare case of CES as the underlying cause of non-bilious vomiting in a 5-month infant. This condition should be considered in the differential diagnosis of recurrent non-bilious vomiting, particularly when associated with faltering growth. Key diagnostic clues were the inability to tolerate solid feeds and the inability to insert a nasogastric tube.

The exact incidence of CES remains uncertain due to limited data, primarily derived from case reports and small case series, as it is often excluded from rare disease registries or categorized under broader groups of oesophageal or gastroesophageal anomalies (10). Estimates suggest an incidence of 1 in 25.000-50.000 live births (3). This data stems from a 1969 retrospective study at the Children's Hospital of Pittsburgh, which identified CES in approximately 10% of patients with tracheoesophageal fistula (24/200) over a period of 15 years. The true incidence of CES may be underreported, as its diagnosis is frequently delayed (3).

Based on histological findings, CES can be divided into three subtypes:

1) Tracheobronchial remnants (TBR): CES caused by TBR is characterised by the presence of ectopic cartilage within the stenotic segment. The cartilaginous tissue may form a ring, or may only be present in a part of the stenosis. Respiratory epithelium with seromucous glands and ciliated columnar epithelium, as well as lymphoid tissue may also be present. This subtype is predominantly found in the lower third of the oesophagus (1,11).
2) Fibromuscular thickening or stenosis (FMS): This form of CES is characterized by circumferential hypertrophy of smooth muscle tissue and submucosal fibrosis. There may also be an abnormal

FIGURE 1: growth curves.

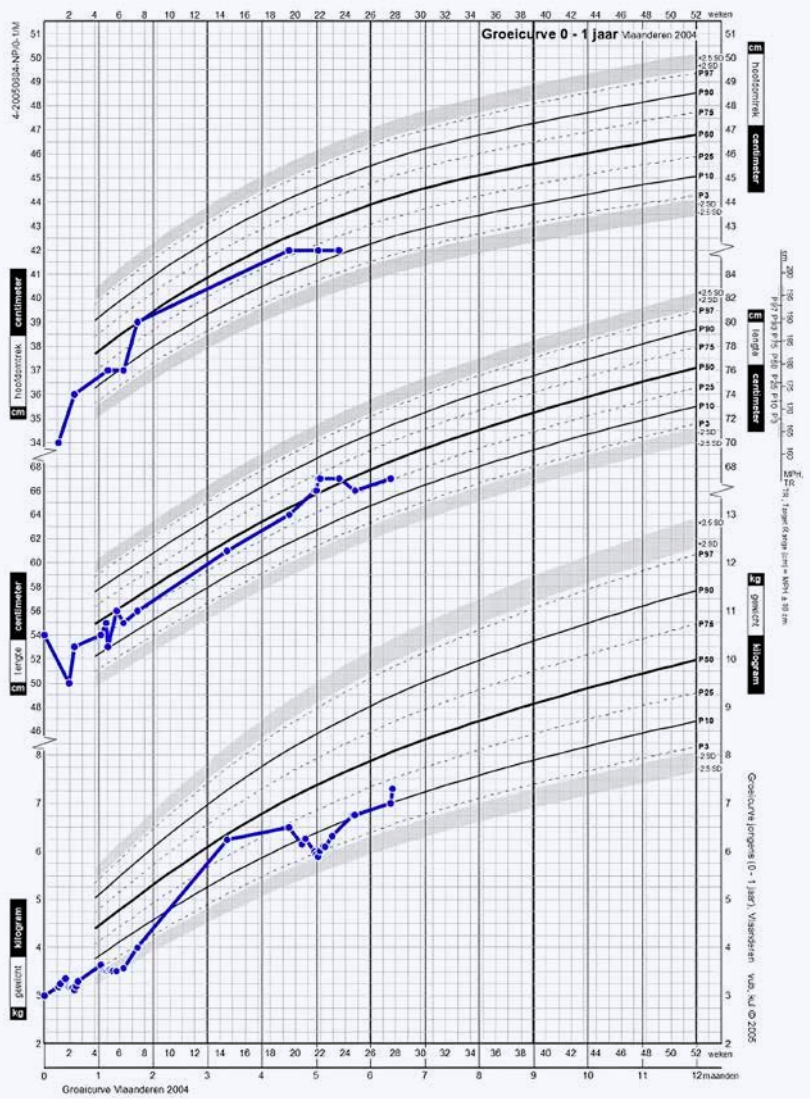


FIGURE 2:

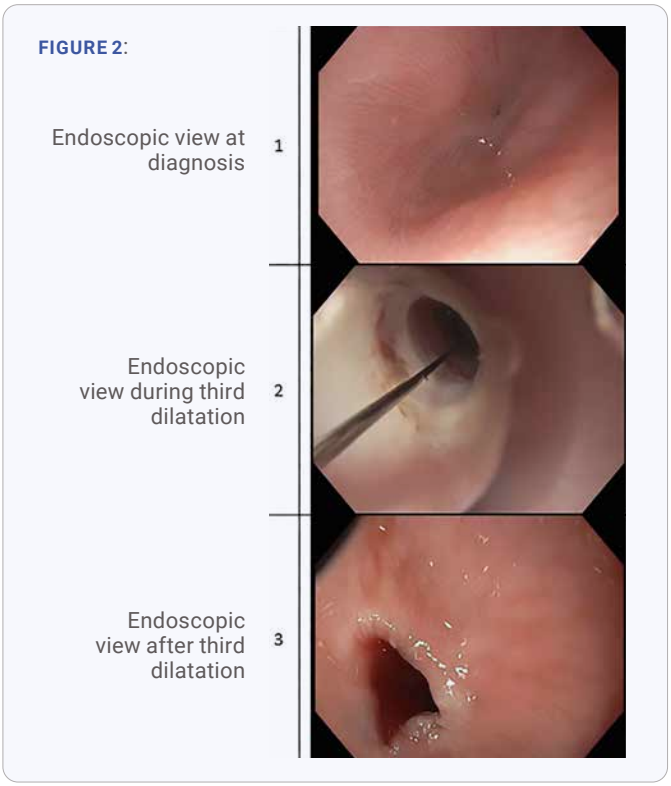
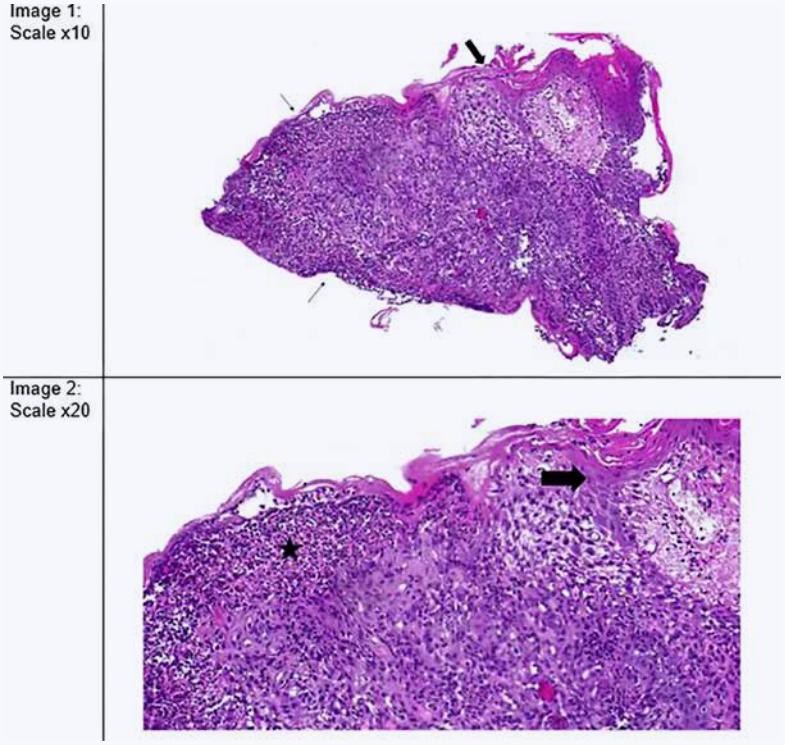


FIGURE 3:

- **Image 1 and 2** show histological images with hematoxylin and eosin stain at 10 and 20 times enlarged scale respectively
- **Image 1**: large arrow indicates reactively changed squamous epithelium. Small arrow shows ulcerative zones with fibrinopurulent material and granulation tissue.
- **Image 2**: large arrow indicated reactively changed squamous epithelium. Asterisk shows ulcerative zone with fibrinopurulent material (abundant granulocytes and some lymfocytes) and underlying granulation tissue



organisation of the muscular layer. This subtype is most commonly found in the middle of lower third of the oesophagus (1,11).

3) Membranous webbing or oesophageal membrane (EM): In this type of CES there is a normal submucosal and muscular organisation of the oesophagus. It mainly is found in the upper and middle third of the oesophagus (1,11).

Histological analysis in our case showed granulation tissue and signs of ulceration (Figure 3), which are non-specific findings. Oesophageal biopsies showed no signs of esophagitis. Due to absence of submucosal of muscular tissue in the biopsies, the subtype of CES could not be confirmed histologically.

Timing and nature of symptoms are determined by the severity of CES. Non-bilious vomiting is a hallmark clinical manifestation, with symptoms often worsening after the introduction of complementary feeding. Other symptoms include faltering growth, dysphagia and food bolus impaction. In cases of severe stenosis, the child may present with hypersalivation, chronic cough, respiratory distress, stridor during feeding, aspiration pneumonia and developmental delay (1,11). In a retrospective multicentre study conducted in France, reporting on 61 patients, 34% were asymptomatic at diagnosis, of the other 40 patients the following symptoms were present at diagnosis: dysphagia in 50%, food impaction in 50%, respiratory symptoms in 42%, and a history of repeated vomiting in 40% (6). Age of diagnosis is variable and delay between first symptoms and diagnosis may be long. (6,8). In less severe cases, symptoms may be more subtle, and diagnosis may only be confirmed later in childhood or even in adulthood (6,12). In the same French multicentre study, age at diagnosis ranged from one day up to 14 years of age, with seven patients who were diagnosed after the age of five years (6). While in another retrospective cohort study, reporting on 20 CES patients (four children with TEF), age of diagnosis ranged between one month and 4.5 years (5). In patients with associated anomalies, diagnosis is often made earlier (6,8).

The diagnosis of CES typically involves imaging techniques such as contrast studies of the upper gastro-intestinal tract, endoscopic ultrasound (EUS), magnetic resonance imaging (MRI) or computed tomography (CT) scan (1,13). EUS is particularly useful to differentiate between CES subtypes. It is especially useful in the identification of TBR, as cartilage is often not identified in biopsies. In FMS it shows hypertrophy of the muscular layer (13,14,15,16). However, successful application of EUS requires a sufficient calibre of the upper oesophageal sphincter and oesophagus to accommodate the passage of the probe. For this reason this investigation was not performed in our case. CT or MRI may also reveal ectopic cartilage in cases of TBR. Upper gastrointestinal endoscopy with biopsies remains the gold standard for diagnosis but may be challenging to distinguish CES from acquired oesophageal stenosis caused by other conditions like reflux esophagitis, eosinophilic esophagitis, caustic ingestion, mediastinal radiation, bullous skin disorders, extrinsic compression and long-term use of nasogastric feeding tubes (1,5,13). Based on the endoscopic, histological, and radiological findings, our case was most compatible with the FMS subtype, as both CT and MRI revealed no evidence of TBR, although we were unable to confirm this histologically.

Treatment of CES varies depending on the subtype and severity of the stenosis. Dilations performed with fluoroscopic or endoscopic guidance or bougienage (based on local expertise and availability of different techniques), are often the first-line treatment (9,13,15,17,18). Surgical repair is reserved as second line treatment, for cases resistant to dilation or complicated by perforation or mediastinitis (12,19). Patients with TBR are more likely to require surgical intervention, as dilations have lower success rates and higher complication rates in this subtype (1,8,11,13,15,20). However, diagnosis of TBR is often challenging, and in several cases, diagnosis is only confirmed in histological investigation after resection.

In a retrospective study reporting on 14 CES patients, 11 patients underwent surgical repair, eight of these patients had prior treatment with dilatations (11). In the French multicentre study, reporting on 61 patients, 16% underwent surgery as primary treatment while 30% underwent surgical repair as secondary treatment after failing dilatations (6). Interestingly, the authors reported that regardless of the type of treatment, 64% of patients continued to experience dysphagia symptoms during follow-up, possibly due to persistent oesophageal dysmotility (6). This advocates a long-term follow-up for these children. A retrospective Italian study involving 47 CES patients, all treated with dilations, reported a perforation rate of 10.6%. Despite this complication, only two patients required surgical intervention due to persistent dysphagia symptoms (17).

Adjuvant therapies, such as local or systemic corticosteroids, local mitomycin C, or proton pump inhibitors, have been used for oesophageal stenosis caused by other aetiologies such as after

oesophageal atresia repair or stenosis due to caustic ingestion, but lack evidence in children with CES (13). In the guidelines for paediatric gastrointestinal endoscopy guidelines by the European Society of Gastrointestinal Endoscopy (ESGE) and European Society of Paediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) stenting and topical mitomycin C are suggested for the treatment of refractory stenosis in benign oesophageal strictures. They do not suggest routine use of intralesional steroids (23). The UK guidelines on oesophageal dilatation in clinical practices advocates for the use of PPI after oesophageal dilatation to decrease of the risk of symptomatic gastro-oesophageal reflux disease or ulcerative esophagitis after this procedure and to avoid recurrence of the stenosis. In this guideline intralesional corticosteroids are mentioned as a possible treatment modality in combination with dilatations in refractory strictures when there is evidence of inflammation and in postoperative strictures however this guideline offers no advice specific for CES (24). Mitomycin C is not advocated in this guideline due to insufficient evidence (24).

Oesophageal stenting may be considered for refractory cases, though its use in CES is rare. A systematic review from 2010 reported no cases of oesophageal stenting in CES, only in case of caustic strictures or strictures following oesophageal atresia repair (21). In an American study reporting on 36 patients, stents were utilized in conjunction with endoscopic incisional therapy (EIT) in 17 patients, and in four patients to address postoperative restenosis. The same study also showed success with the use of EIT in avoiding surgical intervention with an OR of 0.1 (p=0.007) compared to patients who received non-EIT endoscopic therapy. In this case series all patients who went for surgical repair had prior intralesional corticosteroid injections. However, the odds of complications after EIT were significantly greater than in those without EIT (odds ratio 6.39; p< 0.001) (22).

Conclusion

This infant with CES emphasizes the importance of considering this rare entity in cases of recurrent non-bilious vomiting and faltering growth. Invasive diagnostics, including endoscopy, may be required for definitive diagnosis, particularly when symptoms are progressive. Key diagnostic clues in our case included the inability to tolerate solid feeds and failed attempts at nasogastric tube placement.

The authors of this paper have no conflicts of interest to declare.

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