Management of congenital esophageal stenosis associated with esophageal atresia and its impact on postoperative esophageal stricture

Ashraf H.M. Ibrahim[a], Mohamed F. Bazeed[b], Salim Jamil[c], Hamad A. Hader[a], Ibrahim M. Abdel Raheem[a] and Ibrahim Ashraf[a]

Aim **The aim of this work was to study the incidence, management of congenital esophageal stenosis (CES) associated with esophageal atresia (EA) and tracheoesophageal fistula (TEF), and its impact on esophageal stricture (ES) after primary repair.**

Patients and methods **From January 2006 to December 2014, 41 sequential cases of EA with distal TEF were retrospectively studied. Cases with significant ES after primary repair were included in the study. Associated CES was diagnosed in the neonatal period by taking histopathologic samples from the tips of the esophageal pouches, failure to pass a size-6 nasogastric tube distally during primary repair, and by initial esophagogram.**

Results **Significant ES developed in 19 patients (46.3%); of them, six had CES (32%). Three patients had tracheobronchial remnants at the anastomotic site. Two of them had refractory strictures requiring resections and one had mainly major esophageal dysmotility. Patients 4 and 5 had CES distal to the anastomotic site on initial esophagogram. Patient 4 responded well to dilatations, whereas the other one had refractory stricture. Patient 6 had distal CES due to fibromuscular stenosis diagnosed by failure to pass a size-6 nasogastric tube distally. The patient responded well to dilatation, myectomy, and Thal's fundoplication.**

Conclusion **One-third of the patients with significant stricture had CES; half of them were refractory to dilatation. Failure to have histology specimens and a high index of suspicion will make the incidence of this association a rarity. Diagnosis and management of CES with EA/TEF in the neonatal period is possible. Esophageal dilatation is the initial management for all cases with a low threshold for gastric fundoplication and gastrostomy. Resection is reserved for refractory stenosis.** ***Ann Pediatr Surg*** **12:36–42 © 2016 Annals of Pediatric Surgery.**

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[a]Pediatric Surgery Department, [b]Radiology Department and [c]Histopathology Department, Armed Forces Hospital Southern Region, Khamis Mushait, Kingdom of Saudi Arabia

Correspondence to Ashraf H.M. Ibrahim, FRCSI, MD, King Faisal Military City, PO Box 5062, Khamis Mushait, Kingdom of Saudi Arabia
Tel/fax: +966 17 2511180; e-mail: ash_ib@hotmail.com

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Introduction

The incidence of congenital esophageal stenosis (CES) associated with esophageal atresia (EA) ranges from 0.4 to 14% [1–3]. According to four observational studies, the overall incidence of CES among patients with EA and/or tracheoesophageal fistula (TEF) was 9.6% [4]. In a study on 61 patients with CES, 29 had associated EA [5]. CES can affect the anastomotic site [3,6] or distal to it [2,7,8]. The incidence of anastomotic esophageal stricture (ES) after repair of EA ranges from 18 to 50% [9,10]. Most of the cases of ES respond to dilatations, whereas few are refractory, requiring surgical resection. The incidence and impact of CES on postoperative ES is not known. Moreover, there is no consensus as regards the management of CES associated with EA and TEF. The aim of this work was to study the incidence, management of CES associated with EA with distal TEF, and its impact on ES after surgical repair.

Patients and methods

From January 2006 to December 2014, 41 sequential cases of EA with distal TEF were retrospectively studied after obtaining ethical approval from the local committee in Armed Forces Hospital Southern Region, Saudi Arabia. All cases were operated upon by two senior surgeons following the same operative techniques. Significant stricture developed in 19 patients (46.3%) who were actually included in the study. Their charts were reviewed for demographic features, type of surgery, and tension at the anastomotic site. A transanastomotic nasogastric tube insertion and histopathological evaluation of samples from the tips of the upper and lower esophageal pouches were routinely practiced in all cases during primary repair. Postoperative barium swallow and barium meal tests were carried out to study complications such as leakage, recurrent fistula, gastroesophageal reflux (GER), esophageal dysmotility, and ES. All contrast studies were attended by the surgical team. Significant esophageal stricture was diagnosed clinically by means of intolerance to feeds and recurrent respiratory problems supported by esophagogram with more than 50% narrowing of the esophageal lumen in all cases. Stricture on esophagogram was considered severe if the diameter of the esophagus at the stricture site was less than one-third of that of the normal esophagus proximal or distal to it. Otherwise, the stricture was considered mild to moderate. CES at the anastomotic site was defined as histology showing tracheobronchial remnants (TBR) or fibromuscular abnormality consistent with fibromuscular stenosis (FMS). From our previous and present experience [3],

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a histology similar to this will present sooner or later with stenosis and/or esophageal dysmotility. CES distal to the anastomotic site was diagnosed at primary repair either by failure to pass a size 6 nasogastric tube distally or by having a high index of suspicion during initial esophagogram. Repetitive esophageal balloon dilatation every 1 or 2 weeks with gradual step-up was indicated for significant stricture. Wire-guided, pressure-controlled multidiameter balloons (CRE, Boston Scientific Corporation, Massachusetts, USA) were used with fluoroscopic guidance. Esophagoscopy was used only in difficult cases. The outcome was assessed by the response to the number of dilatation sessions, their effectiveness, and complications. A session is composed of three dilatations of 2-min duration each and a 1-min rest interval. The endpoint for dilatation was disappearance of the wasting at the first dilatation of a session and then supported clinically. The response was considered excellent if one session of dilatation was required, satisfactory if up to five sessions were required, and fair if more than five sessions were required. In case of GER with a stricture that does not respond to ineffective dilatations, fundoplication and gastrostomy followed by dilatation are performed. The stricture was considered refractory if surgical resection was indicated due to failure of five dilatation sessions after fundoplication, or the stricture being too tight for a guidewire to pass. During courses of treatment, the dilatation was considered very effective if dysphagea (or intolerance to feeds) disappeared, effective if it was still present to special types of food, or otherwise ineffective.

Results

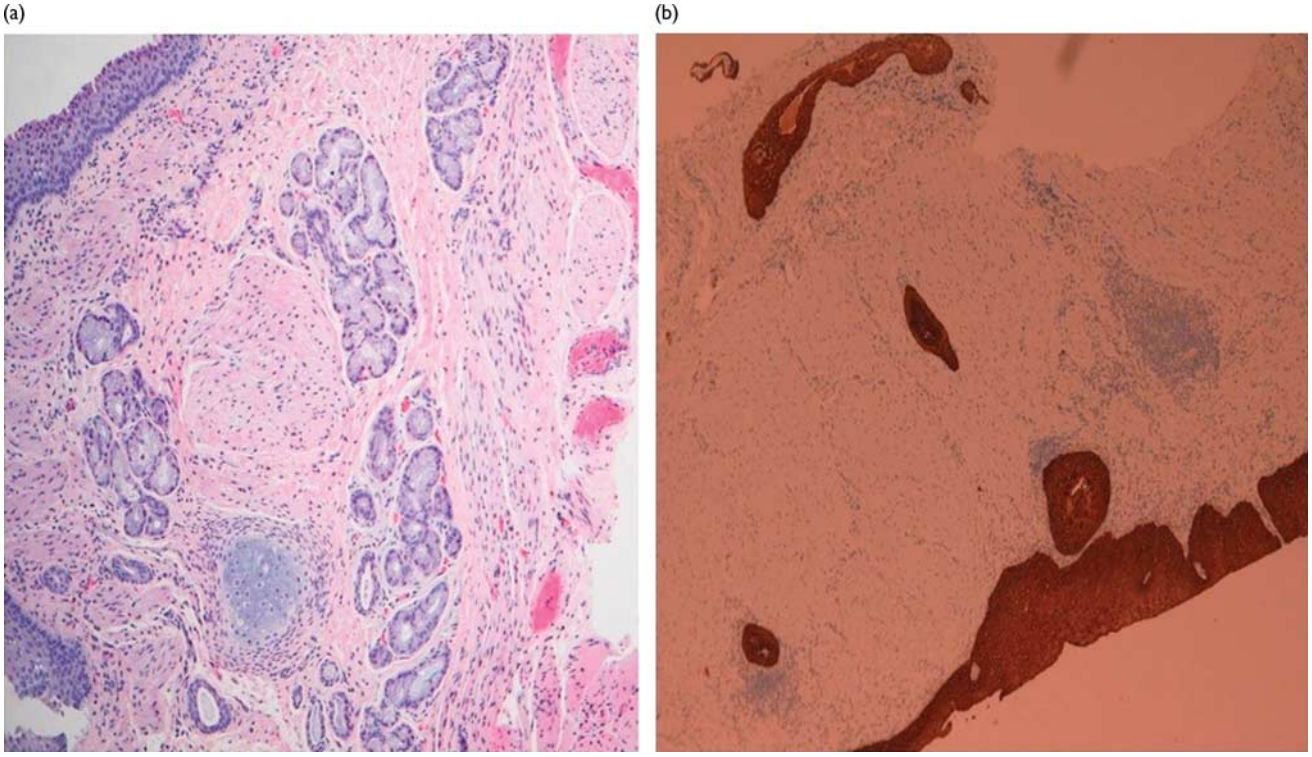
Of the 19 patients with ES, 16 had anastomotic stricture and three distal to it. Their ages at first presentation ranged from 0 to 48 months (median = 3 months). Eleven patients were female and eight were male. Two groups of stricture were identified. The first is the non-CES group, which included 13 patients (68.4%) and the second is the CES group, which included six patients (31.6%). The non-CES group had unremarkable histology. The median age at first dilatation was 5 months (range = 1–48 months). Four patients had initial severe stricture, and the fifth patient had mild-to-moderate initial stricture, which became severe later. One patient had recurrent TEF, one had tense anastomosis, one had major leak, and two patients had minor leaks. Five patients had GER, one responded to conservative treatment and four required Thal's fundoplication with better response to dilatation. Six patients of the non-CES group showed excellent response; six patients showed satisfactory response, and one patient showed initial satisfactory response followed by excellent response after Thal's fundoplication. All patients of this group had very effective dilatations with no complications and a median follow up of 4 years from last dilatation (range = 1–9 years).

Table 1 **CES group with anastomotic and distal stenosis**

Number/ sex	Site of stricture	Degree	Risk factor	Treatment	Age (months)	Number of dilatations	Response to dilatation	Effectiveness/ outcome
1/female	Anastomotic	Severe	TBR/GERD/dysmotility	Dilatation/ARM	2	5	Not applicable	Ineffective
				Thal + GT	4	–	–	–
				Dilatation	5	5	Refractory	Ineffective
				Resection	7	–	–	–
				Dilatation	8	6	Fair	V. effective
				Dilatation	12	5	Satisfactory	V. effective
				Dilatation	24	3	Satisfactory	V. effective
				Dilatation	36	3	Satisfactory	V. effective
				Dilatation	60	3	Satisfactory	V. effective
2/female	Anastomotic	Severe	TBR/GERD/dysmotility	Dilatation/ARM	2	5	Not applicable	Ineffective
				Thal + GT	4	–	–	–
				Dilatation	5	5	Refractory	Ineffective
				Resection	7	–	–	–
				Dilatation	10	7	Fair	V. effective
				Dilatation	16	5	Satisfactory	V. effective
				Dilatation	24	4	Satisfactory	V. effective
				Dilatation	48	2	Satisfactory	V. effective
				Dilatation	72	2	Satisfactory	V. effective
				Dilatation	96	2	Satisfactory	V. effective
3/male	Anastomotic	MM	TBR/GERD/major dysmotility	ARM/dilatation	1	1	Excellent	Ineffective
				Thal + GT + esophageal myectomy	1.5	–	–	Improved
4/male	Distal	MM	? FMD GERD Dysmotility	ARM/dilatation	1	3	Satisfactory	V. effective
				Dilatation	48	2	Satisfactory	V. effective
5/male	Distal	Severe	Dysmotility/? TBR GERD/recurrent TEF	ARM/Thal/GT	1	–	–	–
				Dilatation	3	Too tight	Refractory	Brain insult
				Esophagostomy	24	–	–	Mortality at 36 months
6/female	Distal	Severe	GER Dysmotility FMD/leakage	Dilatation/myectomy/anastomotic tension	0	1	Excellent	V. effective
				Dilatation/myectomy Thal + GT	1			

?, It is valid, as the stenosis is distal, no histological confirmation, but it followed the clinical course of CES; ARM, antireflux measures; FMD, fibromuscular disease; GER, gastroesophageal reflux; GERD, gastroesophageal reflux disease; GT, gastrostomy tube; MM, mild-to-moderate stricture; TBR, tracheobronchial remnants.

Fig. 1



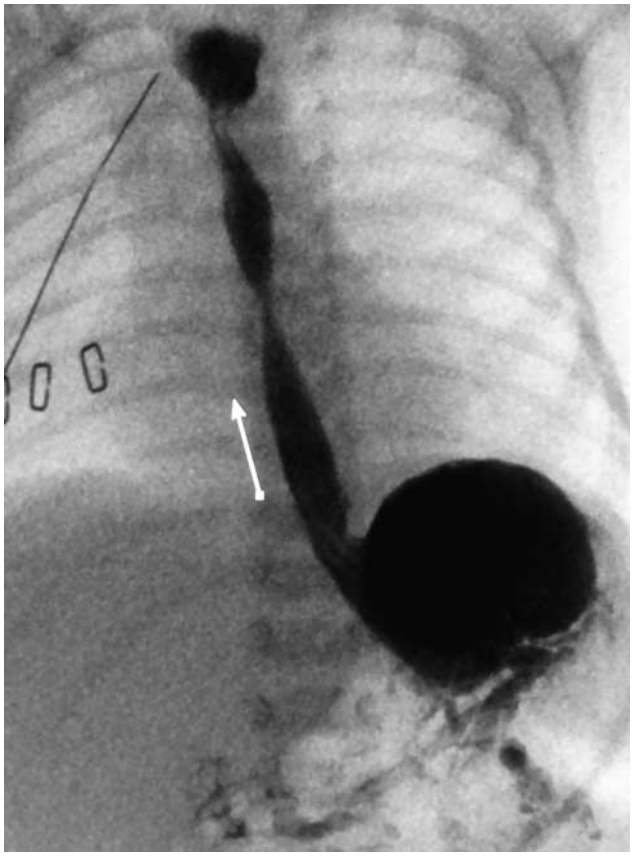
(a) A histological picture of tracheobronchial remnants showing psuedostratified columnar ciliated epithelium, respiratory glands, and cartilage (patients 1, 2, 3). (b) Immunohistochemistry (pancytokeratin, AE1/AE3) of the resected strictured specimens showing squamous epithelium surface (brown) and underlying ducts (brown) inside the muscle layer (blue).

All cases of CES were discovered in the neonatal period but no action was taken, except case number 6, until a clinical and radiological indication for dilatation was obvious. The median age at first dilatation of the CES group was 1 month (range = 0–2 months) (Table 1). Three patients with TBR at the anastomotic site were diagnosed by means of histological examination of the tip of the lower esophageal fistulous end (Fig. 1a). The TBR showed the three elements of respiratory epithelium – namely, psuedostratified columnar ciliated epithelium, respiratory glands, and cartilage. The first and second patients with TBR showed an expected severe anastomotic stricture, which developed at 2 months of age. They also had significant GER and esophageal dysmotility. Both patients had the same scenario of management (Table 1). They underwent surgical resection of the strictured area after failure of dilatation, Thal's fundoplication, and gastrostomy. The resected specimens showed abnormal glands extending into the muscle layer and the adventitia (Fig. 1b). After resection, the response to dilatation was fair to satisfactory and very effective. Recurrent stricture was a prominent feature after prolonged periods of no dysphagea. The third patient of this group with TBR at the anastomotic site had mild-to-moderate anastomotic stricture, which showed a surprisingly excellent response to dilatation. However, the dilatation was ineffective due to major esophageal dysmotility, as the contrast took more than 5 min to pass to the stomach. Because of GER and inability to feed the baby, Thal's fundoplication together with gastrostomy and an extended lower esophageal myectomy were performed with successful outcome. The patient is now feeding orally without gastrostomy for 5 years. The myectomy histology was unremarkable.

Three patients had CES distal to the anastomotic site (patients 4, 5, and 6). Patients 4 and 5 were diagnosed at the initial esophagogram showing a segmental smooth circumferential narrowing in the distal esophagus sparing the gastroesophageal junction (Fig. 2). Patient 4 showed a satisfactory dilatation response at 1 month, but the family was not compliant to dilatation sessions. The last session of dilatation was carried out at 4 years of age with a hugely dilated esophagus (Fig. 3). The dilatation has been considered very effective now for more than 2 years.

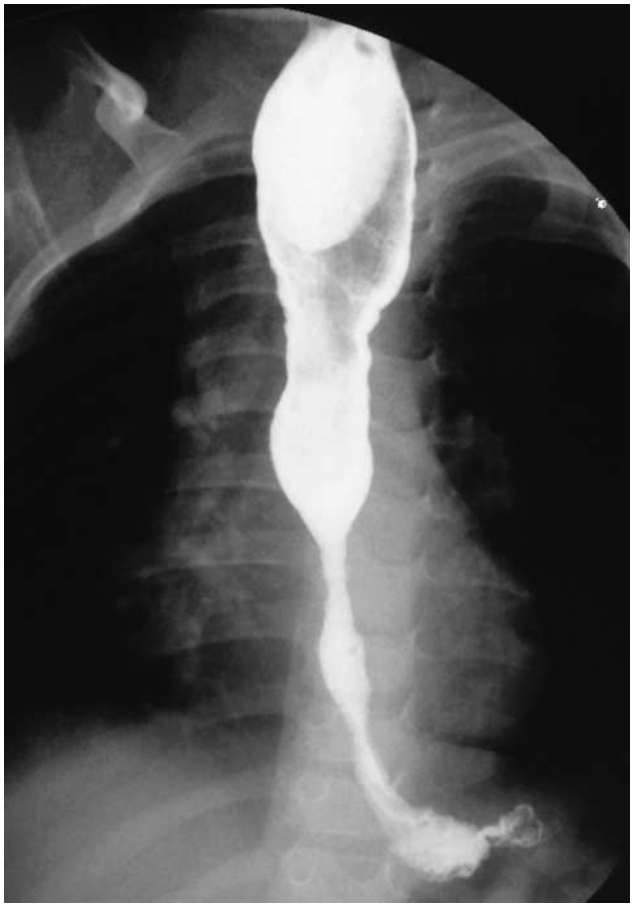
Patient 5 with distal CES was subjected to a contrast study after 9 days of EA repair with a nasogastric tube in the stomach. There was an area of narrowing distal to the anastomotic site together with GER. Nasogastric tube feeding was started with antireflux formula and head-up position. The patient had massive aspiration and required high-frequency ventilation. Repeated contrast studies after weaning from ventilation showed GER and confirmed CES distal to the anastomotic site. Computed tomography of the brain showed severe brain insult. Thal's fundoplication and gastrostomy were performed, through which feeding could be started. At 2 months of age, the stenosis became too tight and this was complicated by recurrent TEF (Fig. 4). Two trials to

Fig. 2



Initial postoperative esophagogram (patients 4 and 5) showing distal CES with segmental smooth circumferential narrowing distal to the anastomotic site and sparing the distal end of the esophagus.

Fig. 3



Esophagogram at 4 years of age (patient 4) showing a hugely dilated esophagus. The patient had a benign clinical course despite being noncompliant to dilatations.

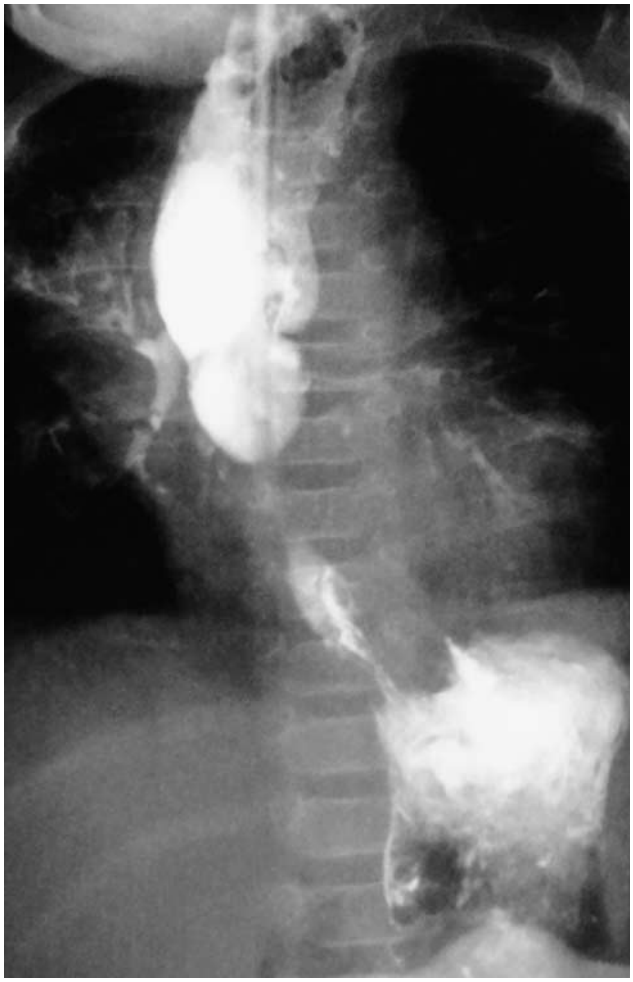
dilate or to pass a guidewire through the stricture to improve saliva swallowing failed, and the stricture was considered refractory. Resection was not advised due to major brain insult. The patient was growing well and finally the father agreed for an esophagostomy to be performed at 2 years of age. The patient died at 3 years of age due to severe sepsis.

Patient 6 with distal CES was diagnosed at primary surgery due to inability to pass a size 6 nasogastric tube distally. A metal probe was used to dilate the obstructed distal esophagus and a size 5 umbilical catheter could be passed to the stomach and the anastomosis was made under tension. Simultaneously, an anterior myectomy of the distal esophagus was performed and sent for histological study. Barium swallow and barium meal tests on the 10th postoperative day showed GER, persistent narrowing distally, and leakage from the anastomotic site. The leakage improved on conservative management but the distal CES persisted, as shown on a repeated esophagogram (Fig. 5). The plan was to continue nasogastric tube pump feeding with antireflux measures for 2 weeks. Balloon dilatation, Thal's fundoplication, gastrostomy, and a complementary transhiatal esophageal myectomy were performed simultaneously (Fig. 6a). Full feeding could be started after a normal esophagogram. The histology of the myectomy specimens showed hypertrophied smooth muscle fibers together with fibrosis indicating FMS (Fig. 6b).

Discussion

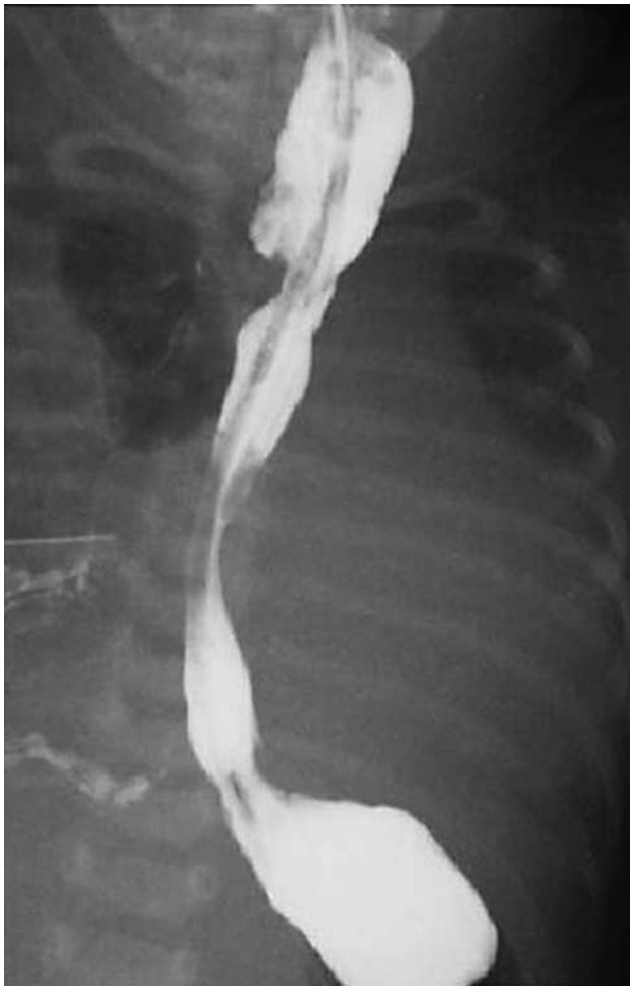
Nihoul-Fékété defined CES as 'an intrinsic stenosis of the esophagus present at birth, although not necessarily symptomatic during the neonatal period, which is caused by congenital malformation of esophageal wall architecture'. Thus, the diagnosis is only confirmed by means of histological studies. He described three entities – namely, TBR, FMS, and the membranous stenosis (MS) [1]. In an extensive review, CES associated with EA was not rare, having an incidence of 9.6%, wherein it could affect the middle (13.5%) or lower third of the esophagus (86.5%) [4]. The authors of the present study believe that the middle third of the esophagus corresponds to the anastomotic site in EA. It has been reported earlier that CES can affect the anastomotic site [3,6] or distal to it [2,7,8]. The diagnosis of CES at the anastomotic site can be confirmed by means of histological examination of specimens obtained from the tips of the esophageal pouches during primary repair of EA [3,6]. CES distal to the anastomotic site is suspected by a segmental, smooth

Fig. 4



Repeated contrast study (patient 5) after Thal's fundoplication showing recurrent TEF and progressing distal CES, which was refractory to dilatation.

Fig. 5

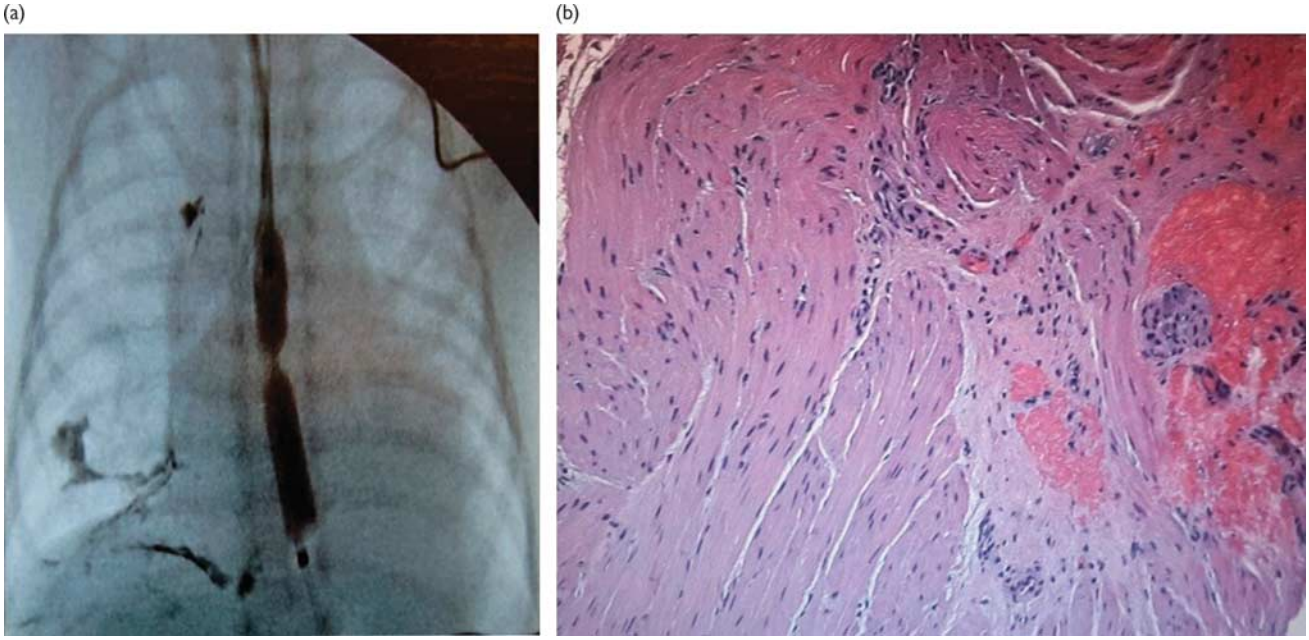


A follow-up barium swallow and meal of the same patient showing cured leakage and a persistent narrowing distal to the anastomotic site; there was also gastroesophageal reflux and dysmotility.

circumferential narrowing in the distal esophagus 2–6 cm above the gastroesophageal junction during esophagogram. Its congenital nature can be confirmed if it is seen in the initial esophagogram soon after EA repair [8]. The incidence of this type of CES is not well documented due to errors in diagnosis [8]. In the present study, the incidence was 7.3% for CES distal to the anastomotic site and 7.3% for the anastomotic type, with an overall incidence of 14.6% among patients with EA and TEF. In a multicenter study [5] as well as in our study, no multiple CES or MS was observed in any patient with EA.

The incidence of anastomotic ES after repair of EA ranges from 18 to 50% [10,11]. In the present study, the incidence was 39%, excluding the three cases with distal CES. Anastomotic ES after EA repair is the most common cause of benign ES [10]. The etiology of ES after repair of EA is not known. Risk factors include anastomotic leakage, tension at the anastomotic site, a two-layer anastomosis, and GER [10,11]. Most of the cases of ES will respond to esophageal dilatation. However, some cases will not respond to dilatation due to a refractory stricture that requires surgical resection. The impact of CES on the response to and efficacy of dilatation is not known. The cause of refractory strictures is said to be related to GER, age at diagnosis, and delayed initiation of dilatation [10,12,13]. In contrast to the CES group, all cases of the non-CES group showed better response to dilatation after antireflux surgery. The authors of the present study would like to add CES as a possible important cause of ES after EA repair and it may partially explain why some of these ES are refractory to dilatation. Patients younger than 6 months of age will respond better to dilatation [10,12]. Early detection and immediate balloon dilatation may prevent scar formation [9]. The time of the first dilatation could be as early as 4 weeks postoperatively [10]. Dilatation before 3 weeks could put the anastomosis at risk for perforation [14]. In the present study, eight patients were younger than 6 months at first dilatation in the non-CES group. Four patients showed excellent response and four showed satisfactory response. All ended up with a very effective dilatation. The total number of dilatations in these patients was 16 sessions (median = 1.5). The CES group did not respect this rule. Although all patients of the CES group were younger than 6 months when dilatation was initiated, three patients were refractory to dilatations. The total

Fig. 6



(a) Chest radiography of the same patient showing remaining distal narrowing during balloon dilatation. The patient also underwent Thal's fundoplication, gastrostomy, and transhiatal myectomy simultaneously. (b) Myectomy specimen (patient 6) with distal CES showing hypertrophic smooth muscle fibers with fibrosis confirming fibromuscular disease.

number of dilatation sessions in this group was 71 (median = 3) (Table 1). Despite the protracted course of dilatations in two TBR patients, one patient is growing well and enjoying a good quality of life with no dysphagea in the prolonged interval periods between dilatation sessions, and the other one did not require dilatations for almost 5 years now. This pattern of outcome makes the follow-up period difficult to assess.

There are some concerns in the management of CES associated with EA. FMS responds better to dilatation, whereas the TBR usually needs resection. TBR can be differentiated by means of histological examination at the anastomotic site or using miniprobe endoscopic ultrasonography. With case selection using endoscopic ultrasonography to differentiate TBR from FMS, a high success rate of balloon dilatation with a low rate of perforation can be achieved [4]. The extent of the anastomotic CES can be very limited or it may extend down to the cardia [3]. Balloon dilatation is an excellent initial diagnostic and therapeutic tool. Most of the cases reported had delayed diagnosis and management [2,4,5,7]. The presentation can be early or delayed for days or months. Some may have a benign course, whereas others may have a very stormy one that might end up with morbidity or even mortality. Recurrent TEF may be a shadow of this pathology due to early postoperative distal obstruction. Careful transanastomotic nasogastric pump feeding should be practiced until balloon dilatation can be performed 3 weeks after primary repair. Isolated CES involves the most distal esophagus including the gastroesophageal junction and behaves exactly like achalasia [15]. In contrast, distal CES associated with EA usually spares the most distal esophagus and gastroesophageal junction and is usually associated with the ominous triad of GER, dysmotility, and stricture. Fundoplication and gastrostomy followed by dilatations may be required. It may be difficult to definitively separate persistent esophageal stricture from esophageal dysmotility in cases of persistent dysphagea [5]. Some authors recommend the need for first-line surgery in patients with TBR [5]. However, the authors of the present study believe that dilatation with an appropriately sized balloon may be the best initial test for a distal CES, its extent, and response to dilatation. Moreover, one of our patients with TBR showed an excellent response to dilatation but that was ineffective due to major esophageal dysmotility. Furthermore, in the patients who responded to dilatation without a proved histological analysis, TBR cannot be excluded [5]. Although MS is not reported in our study, the treatment of MS is straightforward using balloon dilatation and electrocauterization [16].

Conclusion and recommendation

Almost one-third of patients with significant postoperative ES had CES. Diagnosis can be made in the neonatal period. CES may be an important cause of postoperative refractory ES. Dilatation is the initial management for all cases. A low threshold for Thal's fundoplication and gastrostomy is required. Surgical resection followed by dilatation is reserved for refractory strictures after antireflux surgery or inability to dilate. The authors recommend that early neonatal diagnosis can be made by means of routine histopathology of specimens and having a high index of suspicion during initial esophagogram. Balloon dilatation, as a diagnostic and therapeutic procedure, should begin at the age of 3–4 weeks after primary repair even before symptoms develop. Until that age, careful transanastomotic pump feeding is recommended.

Acknowledgements

Conflicts of interest

There are no conflicts of interest.

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