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ORIGINAL ARTICLE

Current characteristics and management of congenital esophageal stenosis: 40 consecutive cases from a multicenter study in the Kyushu area of Japan

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Abstract
Purpose Congenital esophageal stenosis (CES) is rare, and the available clinical data are limited. We explored the current diagnosis, treatment and outcomes of CES.
Methods A questionnaire survey was performed using medical records at pediatric surgical centers in the Kyushu area.
Results Over 10 years, 40 patients (24 males) had CES. The incidence of associated anomalies was 52.5% (21/40), and that of esophageal atresia was 20.0% (8/40). The mean age at the diagnosis was 12.0 months (range, 1 day–8.8 years). Seven (17.5%) patients were diagnosed in the neonatal period. Ten (25.0%) developed CES due to tracheobronchial remnants, 27 (67.5%) due to fibromuscular stenosis (FMS) and 1 (2.5%) due to membranous stenosis + FMS. Thirty-six (90.0%) were treated by balloon dilatation (mean, 3 times; range, 1-20). Perforation at dilatation occurred in 7 (17.5%) patients, and all were diagnosed with FMS. Eighteen (45.0%) patients underwent radical operation (3 primary, 15 secondary to dilatation).
Conclusions Our study clarified the characteristics and outcomes of CES, including neonatal diagnoses. CES occurred in 1 in every 33,000 births in the Kyushu area. Careful attention should be paid, even in cases of dilatation for FMS. CES requires long-term follow-up for symptom persistence after adequate and repeated treatment.

Keywords Congenital esophageal stenosis · Neonate · Dilatation · Perforation

Introduction

Congenital esophageal stenosis (CES) is an extremely rare condition and has been reported to occur once in every 25,000–50,000 births [1], although the true incidence remains unknown. Nihoul-Fekete et al. [2] reported the following entities under the category of CES: ectopic tracheobronchial remnants in the esophageal wall (TBR), segmental fibromuscular hypertrophy of the muscle and submucosal layers (FMS) and a membranous diaphragm or stenosis (MS). This classification is now broadly accepted. The incidence of associated anomalies was reported to range from 17 to 33% [3]. CES is frequently associated with esophageal atresia (EA) [4].

Symptoms of CES usually begin in infancy with progressive dysphagia and vomiting, generally after the introduction of semisolid or solid foods around 6 months of age [3]. It is generally treated mainly with dilatation and operation. Balloon dilatation is usually selected at first, but its utility varies among cases. In addition, the risk of perforation remains. Radical operation is carefully selected for cases unresponsive to dilatation [5]. A definitive determination of the type of CES before treatment is often difficult. In addition, few data are available regarding the treatment and outcomes of CES from small series [6–8].

The aim of this study was to clarify the current diagnosis, treatment and outcomes of CES in the Kyushu area of Japan over the past decade.

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Methods

We sent questionnaires to the Departments of Pediatric Surgery at representative institutions throughout the Kyushu area of Japan. The questionnaires were designed to collect data on the diagnosis, treatment and outcome of CES over the past decade (2005–2014). This clinical study was approved by the Institutional Review Board of our institution (20160107).

Twenty-one out of 29 institutions (72.4%) responded to our questionnaires. Data were collected on 40 patients. These data were obtained retrospectively from the patients' clinical, radiological, endoscopic and operative records. We analyzed the patient background characteristics, associated anomalies, age of onset, clinical symptoms, age of diagnosis, diagnostic approach, treatment and outcome. The associated anomalies involved chromosomal abnormalities, congenital heart disease, congenital malformation of central nervous system, head and neck, respiratory, gastrointestinal, urogenital, body surface, limb and others. Gross's classification of EA was used. Symptoms included vomiting, respiratory symptoms, dysphagia and food impaction. The diagnostic modalities included contrast esophagogram, esophagoscopy, esophageal manometry, pH monitoring, computed tomography (CT) and endoscopic ultrasonography (EUS). Contrast esophagography findings were also classified concerning the form (abrupt or tapered or other) and location. The therapeutic treatments included balloon dilatation and radical operation. The results of dilatation were analyzed in detail (frequency, perforation and outcome). Pathological evaluation was performed in the case that underwent radical operation.

Results

Patients' background and clinical data

The data of 40 CES patients were collected from the responding institutions. The incidence of CES was estimated at roughly 1/33,000 live births. During this study period, a total of 1,328,925 births were reported in the Kyushu area of Japan.

Patients' background and clinical data are shown in Table 1. There were 24 males and 16 females. Regarding the gestational age, 10 (25.0%) were born at <37 weeks. Fifteen (37.5%) patients weighed <2500 g at birth. The mean birth weight was 2590 g (range 1137–3700 g). Fourteen patients (35.0%) presented with symptoms within 6 months of birth, and 9 patients (22.5%) received a definitive diagnosis. Five patients (12.5%) had symptoms in the neonatal period. Seven (17.5%) patients were diagnosed in the neonatal period. Four patients with CES (10.0%) did not present with any symptom at the time of the diagnosis: one patient was diagnosed incidentally during surgical repair of EA; one patient was diagnosed incidentally during surgical repair of duodenal atresia at 3 days old; the other two patients had CES diagnosed on follow-up esophagogram after repair of EA at 8 and 28 days old (1 each).

Table 1 Patients' background and clinical data

Sex (M:F)	24:16
Gestational age	
<37 weeks	10/40 (25.0%)
≥37 weeks	23/40 (57.5%)
Unknown	7/40 (17.5%)
Birth weight	
<2500 g	15/40 (37.5%)
≥2500 g	20/40 (50.0%)
Unknown	5/40 (12.5%)
Age at symptom onset (month)	
<1	5/40 (12.5%)
1–6	9/40 (22.5%)
>6	22/40 (55.0%)
Asymptomatic	4/40 (10.0%)
Age at diagnosis (month)	
<1	7/40 (17.5%)
1–6	2/40 0(5.0%)
>6	27/40 (62.5%)
Unknown	4/40 (10.0%)
CES with EA	8/40 (20.0%)
Growth retardation at diagnosis	10/29 (34.5%)

Thirty-six patients (90.0%) presented with symptoms at a mean age of 7.0 months (range 5 days–45 months). Their symptoms included vomiting (33/40, 82.5%), respiratory symptoms (12/40, 30.0%), dysphagia (8/40, 20.0%) and food impaction (8/40, 20.0%). The mean age at the diagnosis was 12.0 months (1 day–8.8 years). Growth retardation <−2.0 standard deviation was recognized in 10 (34.5%) of 29 patients whose body weight had been recorded.

Associated anomalies

Associated anomalies were recognized in 21 (52.5%) of the 40 patients and are summarized in Table 2. A total of 34 associated anomalies were recognized in 21 patients. Nine patients had two associated anomalies, and two patients had three associated anomalies. EA was recognized in 8 cases (20.0%, Gross A: 2 cases, Gross C: 6 cases). Down's syndrome was recognized in two cases.

Location and type of CES

Contrast esophagogram was performed in all patients. Two patients had two sites of stenosis. The esophagogram showed

Table 2 Associated anomalies

Gastrointestinal	13
Esophageal atresia (Gross A)	2
Esophageal atresia (Gross C)	6
Gastric volvulus	1
Duodenal atresia	1
Malrotation	1
Imperforated anus	2
Cardiovascular	5
Urogenital	3
Chromosomal (down's syndrome)	2
Other	11
Total	34

the shape of the stenosis with abrupt narrowing in 16/42 (38.1%), tapered narrowing in 17/42 (40.5%), a flask-shape shadow in 1/42 (2.4%) and no description in 8/42 (19.0%).

Esophagoscopy was performed in 33 patients (82.5%). Esophagoscopy showed stenosis without inflammation in 28 patients. Reflux esophagitis was recognized in only one patient associated with EA. In 20 patients, the endoscope could not pass through the stenosis. EUS was performed in five patients. Based on the EUS findings, TBR was recognized in one patient and FMS in three patients. PH monitoring was performed in 10 patients. Gastroesophageal reflux (GER) was recognized in four patients. Esophageal manometry was performed in five patients and showed no findings of achalasia. CT was performed in 17 patients and showed a narrow segment of the esophagus in 3 and wall thickening of the esophagus in 3. A pathological evaluation for the stenosis was carried out in 18 patients after radical operation. TBR were found in 10 patients. FMS was found in seven patients. Scar stenosis was found in one patient. The esophagogram findings in patients who underwent radical operation were as follows: 10 with abrupt narrowing (7 TBR and 3 FMS), 3 with tapered narrowing (1 TBR and 2 FMS) and 5 with unknown findings (2 TBR, 2 FMS and 1 scar). The EUS findings in patients who underwent radical operation were as follows: 1 with cartilage in the esophageal wall (1 TBR) and 2 with muscle hypertrophy without cartilage in the esophageal wall (2 FMS). The correlation of esophagogram findings and the diagnosis was as follows: 16 with abrupt narrowing (8 TBR, 6 FMS, 1 MS and 1 unknown), 17 with tapered narrowing (2 TBR, 13 FMS and 2 unknown) and 1 with flask-shape shadow (1 TBR).

The location and type of CES are summarized in Table 3. The location of the 42 stenoses was as follows: upper in 1 (2.4%), middle in 3 (7.1%), lower in 26 (61.9%) and cardia in 12 (28.6%). The type of the 42 stenoses was as follows: TBR in 11 (26.2%), FMS in 28 (66.6%), MS in 1 (2.4%) and unknown in 2 (4.8%).

Table 3 Location and type of CES

	Upper	Middle	Lower	Cardia	Total
FMS		3	18	6	27
TBR			3	6	9
TBR + TBR			2		2
MS + FMS	1 (MS)		1		2
Unknown			2		2
Total	1	3	26	12	42

FMS segmental fibromuscular hypertrophy of the muscle and submucosal layers, *TBR* ectopic tracheobronchial remnants in the esophageal wall, *MS* membranous diaphragm or stenosis

Type of CES and treatment

The type of CES and treatment are summarized in Table 4. Thirty-six patients (90.0%), including 7 TBR, 26 FMS, 1 TBR + TBR, 1 MS + FMS and 1 unknown, were initially treated by balloon dilatation. The mean number of dilatations per patient was 3 (range 1–20). The mean age at the first dilatation was 13.0 months (range 2.9 months–8.8 years). Perforation was recognized in 7 FMS patients. The mean number of dilatations for each patient was 2.4 (range 1–7) in the seven perforated FMS patients. Five patients were treated conservatively. Two patients required drainage: one by thoracotomy and the other by thoracoscopy. Balloon dilatation was effective in six patients despite perforation. Radical operation was performed in one patient after dilatation. Two patients still had dysphagia. Eight TBR patients (one with a double TBR region) underwent balloon dilatation. The mean number of dilatations for each patient was 5.3 (range 2–20). Balloon dilatations were not effective in all TBR patients. Primary radical operation was performed in three patients (two TBR, one FMS). Radical operation after dilatation was performed in 15 patients (7 TBR, 6 FMS, 1 TBR + TBR and 1 unknown).

Treatment and outcomes

The ultimate outcomes are shown in Fig. 1. All patients survived. Twenty-six patients (65.0%) had no symptoms. However, 13 patients (32.5%) still had symptoms after treatment. One patient was diagnosed and underwent treatment at another institution (details unknown). Radical operation was performed in 18 patients, including three primary and 15 after dilatation. The approach for radical operation was as follows: 13 thoracotomies (6 right, 7 left), three thoracoscopic surgeries and two laparotomies. Fundoplication was added in three patients. The procedures for radical operation were as follows: 14 segmental resections of the stenotic site and end-to-end anastomosis and four myotomies. Fifteen (83.3%) of the 18 patients

Table 4 Type of CES and treatment

	TBR	FMS	TBR + TBR	MS + FMS	Unknown
Patient number	9	27	1	1	2
Balloon dilatation	7/9 (77.8%)	26/27 (96.3%)	1/1 (100%)	1/1 (100%)	1/2 (50.0%)
Perforation by dilatation	0/7 (0%)	7/26 (26.9%)	0/1 (0%)	0/1 (0%)	0/1 (0%)
Primary operation	2/9 (22.2%)	1/27 (3.7%)	0/0 (0%)	0/0 (0%)	0/0 (0%)
Radical operation after dilatation	7/9 (77.8%)	6/27 (22.2%)	1/1 (100%)	0/0 (0%)	1/2 50.0%)
Persistent symptoms	6/9 (66.7%)	7/27 (25.9%)	0/1 (0%)	0/0 (0%)	1/2 (50.0%)

FMS segmental fibromuscular hypertrophy of the muscle and submucosal layers, *TBR* ectopic tracheobronchial remnants in the esophageal wall, *MS* membranous diaphragm or stenosis

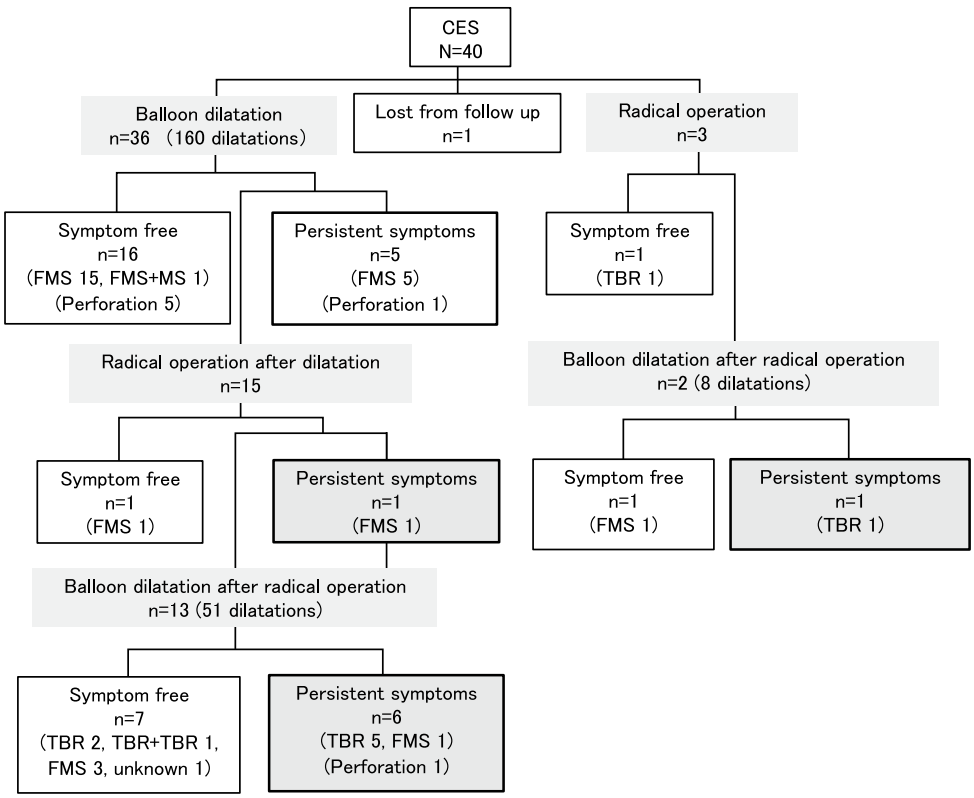

Fig. 1 Treatment and outcome. This flow chart shows the treatment and outcomes for CES

who underwent radical operation required balloon dilatation. As a result, eight patients (44.4%) still had symptoms even after radical operation. Persistent symptoms were as follows: four cases of dysphagia, four of vomiting, two of growth retardation, one of stridor and one of chest discomfort. Two patients had three persistent symptoms.

Discussion

In this study, we clarified the characteristics and management of congenital esophageal stenosis in the Kyushu area of Japan. The major findings of this study were as follows: (1) CES occurred in 1 in every 33,000 births; (2) CES was diagnosed even in the neonatal period; (3) all cases of perforation by balloon dilatation were recognized in FMS patients; (4) More than 40% of patients still had symptoms even after radical operation.

The true incidence of CES is still unknown, although CES has been reported to be a rare condition [5]. Bluestone et al. [1] treated 24 cases of CES and approximately 200 cases of EA in a single institution during the same 15-year period. They estimated that the incidence of CES was 1/25,000 births based on the incidence of EA (1/2500 live births). Nihoul-Fekete et al. [2] identified 20 cases of CES and 484 cases of EA in a single institution during the same 25-year

period. According to that report, the incidence of CES was <1/20 of that of EA. Therefore, CES has been reported to occur at rates of 1 in every 25,000 to 50,000 births [5]. The reported incidences of CES above were based on the incidence of EA.

However, Nishina et al. [9] collected 81 cases of TBR and reported a possibly higher incidence of CES in Japan than noted in other reports. In our study, 40 CES patients were collected from the responding institutions. This number is almost equal to the true patient numbers of CES in the Kyushu area during this research period. We estimated the incidence in the Kyushu area by direct calculation using the total number of births in the Kyushu area. The obtained incidence of CES in the Kyushu area is therefore suspected to be reliable because most major pediatric surgery institutions with CES cases responded to our survey.

CES is usually diagnosed after the introduction of solid food, so it is rarely diagnosed in the neonatal period [8]. However, 7 patients (17.5%) were diagnosed in the neonatal period in the present study. Of the seven neonatal diagnosed cases, four were diagnosed incidentally during an operation for an associated disease (EA in one and duodenal atresia in one) or during follow-up esophagogram (for EA in two). In addition, five patients (12.5%) had symptoms in the neonatal period. These data suggest that we should consider the possibility of CES, even in the neonatal period.

Regarding the incidence of EA in CES patients, Terui et al. [5] reported a rate of 24.8% (82/331; range 0–75%) in their systematic review [1, 2, 5–13]. In our data, the incidence rate of EA in CES was 8/40 (20.0%). During the same period, 198 patients were treated for EA in the responding institutions. The incidence of CES in EA was therefore 8/198 (4.0%). Regarding the incidence of CES in EA patients, Terui et al. [5] reported a rate of 9.6% (55/571; range 5.1–13.8%) in their systematic review [4, 5, 14–16]. Pediatric surgeons should consider the possible association of CES when treating EA patients.

An esophagogram is used as the primary diagnostic modality. However, Amae et al. [13] reported that the outcome of the esophagogram was not related to the histological findings. We obtained similar results in our study and concluded that tapered narrowing was significantly correlated with FMS, but abrupt narrowing did not always correlate with TBR.

The type of CES is important for determining the therapeutic strategy [5], and EUS is a useful tool for determining the type of CES [5]. However, only a few patients (12.5%) underwent EUS in our study. EUS is not a common diagnostic modality in pediatric patients, depending on the institution, but should be used to classify CES before treatment whenever possible.

Regarding the definitive diagnosis of type of CES, the pathological diagnosis was primarily used. However, in cases in which no pathological findings were available, the type of CES was carefully determined based on the contrast esophagogram findings, EUS findings and the efficacy of balloon dilatation. We defined "unknown" as cases in which contrast definitive esophagogram findings and a pathological diagnosis were not obtained on a questionnaires survey. Three patients who were diagnosed as TBR preoperatively were primarily treated by radical operation. As a result, the definitive diagnosis of one patient was changed from TBR to FMS based on pathological findings.

Cases of TBR should be treated with radical operation because of the inefficacy of dilatation and the risk of perforation [17]. In general, balloon dilatation is an effective treatment for MS and FMS. In the present study, 16/36 patients (44.4%) had no symptoms after balloon dilatation. However, the risk of perforation with balloon dilatation is higher than expected, as shown in the data from the present study. Perforation occurred mostly with the first or second dilatation. In general, balloon dilatation was performed at 3–8 atmosphere, three times (3-min duration and 1-min interval). The pressure and number of dilatations were modified depending on the patient. Careful attention should therefore be paid even when performing dilatation for FMS, especially in the early stage of dilatation. The definitive diagnosis of the type of CES before treatment using the combined diagnostic modalities of contrast esophagogram, EUS and CT is important for appropriate treatment. Balloon dilatation is the first choice for MS and FMS, with care taken to avoid perforation. For TBR, radical operation should be considered. Resection of the stenotic region and anastomosis is the most common procedure. However, symptoms may remain even after radical operation, so long-term follow-up is necessary to ensure patients' healthy growth and development.

Michaud et al. [6] reported on the efficacy of radical operation for CES. They noted that 24/61 (39.3%) of CES patients underwent radical operation, but 16/24 (66.7%) still had stenotic symptoms. In contrast, Amae et al. [13] reported the effectiveness of radical operation. They observed 10/14 (71.4%) CES patients who underwent radical operation. Eight of these patients were followed up at their outpatient clinic, and all of the patients were able to eat solid or semisolid food without any symptoms. Our study showed that 15/18 patients (83.3%) required balloon dilatation after radical operation, and 8/18 patients (44.4%) still had symptoms, as shown in Fig. 1. Radical operation is therefore not always a definitive curative option for CES patients in our study.

One limitation of this study is the lack of long-term outcomes, including problems associated with growth retardation.

Our data were based on the short-term results, so the long-term results should be clarified in another study.

In conclusion, we clarified the current status regarding the diagnosis, treatment and outcome for CES in the Kyushu area of Japan. The treatment outcomes of CES are not yet satisfactory, as symptoms persist even after adequate and repeated treatment in many patients. Further studies regarding the therapeutic improvement and long-term follow-up are required.

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Compliance with ethical standards

Conflicts of interest None.

Appendix

Fukuoka Children's Hospital	Fukuoka
Fukuoka University	Fukuoka
Japan Community Health care Organization Kyushu Hospital	Kitakyushu
Japanese Red Cross Kumamoto Hospital	Kumamoto
Kagoshima City Hospital	Kagoshima
Kagoshima University Graduate School of Medical and Dental Sciences	Kagoshima
Kitakyushu Municipal Medical Center	Kitakyushu
Kumamoto City Hospital	Kumamoto
Kumamoto University Hospital	Kumamoto
Kurume University School of Medicine	Kurume
Kyushu Medical Center	Fukuoka
Kyushu University Hospital	Fukuoka
Miyazaki University Hospital	Miyazaki
Nagasaki University Hospital	Nagasaki
Oita Children's Hospital	Oita
Oita Prefectural Hospital	Oita
Oita University Hospital	Oita
Okinawa Prefectural Nanbu Medical Center and Children's Hospital	Naha
Shimonoseki City Central Hospital	Shimonoseki
University of Occupational and Environmental Health	Kitakyushu
University of the Ryukyus	Naha

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