Journal of Pediatric Surgery 49 (2014) 1799–1803

Contents lists available at ScienceDirect

Journal of Pediatric Surgery

journal homepage: www.elsevier.com/locate/jpedsurg

Pediatric chronic intestinal pseudo-obstruction is a rare, serious, and intractable disease: A report of a nationwide survey in Japan ☆

Mitsuru Muto [a,1,*], Hiroshi Matsufuji [a,1], Takeshi Tomomasa [b,1], Atsushi Nakajima [c,1], Hisayoshi Kawahara [d,1], Shinobu Ida [e,1], Kosuke Ushijima [f,1], Akio Kubota [g,1], Sotaro Mushiake [h,1], Tomoaki Taguchi [i,1]

[a] Department of Pediatric Surgery, Kagoshima University, Japan
[b] PAL Children's Clinic, Japan
[c] Division of Gastroenterology, Yokohama City University School of Medicine, Japan
[d] Department of Pediatric Surgery, Hamamatsu University School of Medicine, Japan
[e] Department of Pediatric Gastroenterology, Nutrition and Endocrinology, Osaka Medical Center and Research Institute for Maternal and Child Health, Japan
[f] Kurume University Medical Center, Japan
[g] Second Department of Surgery, Wakayama Medical University, Japan
[h] Department of Pediatrics, Nara Hospital Kinki University, Japan
[i] Department of Pediatric Surgery, Kyushu University, Japan

ARTICLE INFO

Article history:
Received 20 August 2014
Accepted 5 September 2014

Key words:
Chronic intestinal pseudo-obstruction
CIPO
Children
Nationwide survey
Idiopathic

ABSTRACT

Background/Purpose: A nationwide survey was conducted to identify the clinical presentation of pediatric chronic intestinal pseudo-obstruction (CIPO) in Japan.
Methods: Data were collected via a questionnaire, ensuring patient anonymity, from facilities that treat pediatric gastrointestinal diseases in Japan.
Results: Ninety-two responses were collected from forty-seven facilities. Sixty-two patients (28 males, 34 females) met formal diagnostic criteria for CIPO. The estimated pediatric prevalence was 3.7 in 1 million individuals. More than half the children (56.5%) developed CIPO in the neonatal period. Full-thickness intestinal specimens were available for histopathology assessment in forty-five patients (72.6%). Forty-one (91.1%) had no pathological abnormalities and were considered to be idiopathic. Patients were treated according to the local protocol of each facility. Forty-one patients (66.1%) had restricted oral intake of ordinary diets, and twenty-nine (46.8%) depended on parenteral nutrition. No therapeutic intervention, including medication and surgery, successfully improved oral food intake or obstructive symptoms. Only three patients (4.8%) died from enteritis or sepsis.
Conclusions: In Japan, pediatric CIPO is a rare, serious, and intractable disease. The prognosis with respect to survival is good, but unsatisfactory because of the need for prolonged parenteral nutrition and associated potential for restricted quality of life.

Intestinal pseudo-obstruction was first described in 1958 [1]. Dudley et al. first reported patients with serious symptoms and signs of intestinal obstruction, yet without frank mechanical obstruction. The term *chronic intestinal pseudo-obstruction* (CIPO) was proposed by Christensen et al. in 1978 [2]. In children, CIPO has been variously termed, chronic intestinal pseudo-obstruction (CIP), chronic intestinal pseudo-obstruction syndrome (CIPS or CIPOS), pseudo-Hirschsprung's disease, and chronic adynamic ileus [3–7].

The diagnosis of CIPO is made by recognition of prolonged obstructive symptoms and exclusion of mechanical obstruction. New diagnostic criteria and appropriate management strategies for adult CIPO have been proposed for Japan [8,9]. However, review of diagnostic criteria for pediatric CIPO is warranted. In addition, very little is known about the epidemiological and clinical features of CIPO among children in Japan. Therefore, a nationwide study was conducted to assess the present status of the disease.

1. Materials and methods

In February 2012, a survey was sent to facilities represented by members of the Japanese Society of Pediatric Surgeons; the Japanese Society for Pediatric Gastroenterology, Hepatology and Nutrition; and the Japanese Study Group of Pediatric Constipation. Information on patient demographics, clinical features, examination findings, drug treatments and surgical treatments were solicited (see Table 1).

☆ Pediatric CIPO, Research Group for "Comprehensive Study and Seamless Guidelines" on rare and intractable gastrointestinal disease from childhood, supported by the Ministry of Health, Labor and Welfare of Japan.

* Corresponding author at: Department of Pediatric Surgery, Kagoshima University, 8-35-1 Sakuragaoka, Kagoshima, 8908520 Japan. Tel.: +81 99 275 5444; fax: +81 99 275 2628.
E-mail addresses: mitsuru@m3.kufm.kagoshima-u.ac.jp, mitsuru_muto@yahoo.co.jp (M. Muto).

[1] Japanese Study Group of Allied Disorders of Hirschsprung's disease.

http://dx.doi.org/10.1016/j.jpedsurg.2014.09.025
0022-3468/

Table 1
Main questionnaires in the nationwide survey on pediatric CIPO in Japan.

Basic informations	
Day of birth	(yyyy.mm.dd
Gender	☐Male ☐Female
Gestation	w d
Birth weight	g
Onset	☐Neonatal (<30 d) ☐Infancy (1 to 12 m) ☐Childhood (1 y to <7 y) ☐School age or later
Familial incidence	☐Present ( ) ☐Absent
Initial symptom (multiple answers allowed)	☐Abdominal distension ☐Vomiting ☐Delayed meconium excretion (>24 h after birth) ☐Chronic constipation ☐Abdominal pain ☐Enteritis ☐Diarrhea ☐Megacystis ☐Prenatally diagnosed abnormality (if any) ☐Others (free statement)
Affected lesions (multiple answers allowed)	☐Stomach ☐Duodenum ☐Jejunum ☐Ileum ☐Appendix ☐Cecum ☐Ascending colon ☐Transverse colon ☐Descending colon ☐Sigmoid colon ☐Rectum ☐Anus ☐Unknown
Associated malformation	☐Present ( )
Examinations	
Abdominal Xray (multiple answers allowed)	☐Dilatation ☐Air fluid levels ☐Pneumoperitoneum ☐Others
Contrast enema (multiple answers allowed)	☐Normal ☐Microcolon ☐Megacolon ☐Caliber change ☐Unknown ☐Others
Anorectal reflex	☐Positive ☐Atypically positive ☐Negagive
Rectal suction biopsy (AChE staining)	☐Normal ☐Proliferation of AchE-positive fibers ☐Giantganglia ☐Ectopic ganglia
Medication drugs used for treatments	☐Probiotics (; effective / ineffective) ☐Kampo (; effective/ ineffective) ☐Laxatives (; effective / ineffective) ☐Prokinetic drugs (; effective / ineffective)
Surgical treatments	☐Gastroenterostomy ☐No decompression surgery ☐Stoma closure ☐Small bowel transplantation ☐Unknown
Final pathological findings from excised or biopsy specimens	☐Normal ☐Abnormal (findings:)
Current nutritional management (multiple answers allowed)	☐Usual diet ☐Semidigested diet ☐Formula diet ☐Parenteral nutrition
Clinical outcome	☐Alive / ☐Died (yyyy.mm.dd) (cause of death:)

Survey responses were compiled into a database, ensuring anonymity of the respondents, and subsequently analyzed. We divided the reported patients into the following 2 groups: those who developed CIPO during the neonatal period and those who developed CIPO after the neonatal period. In our analysis, we adopted the definition of pediatric CIPO mentioned by Rudolph et al. in 1997 [3]: "pseudo-obstruction denotes signs and symptoms resembling a physical obstruction to luminal flow, including radiographic documentation of dilated bowel with air fluid levels, in the absence of a true mechanical obstruction." The disease is considered to be "chronic" if pseudo-obstruction occurs during the neonatal period and persists for the first 2 months of life or if it occurs after the neonatal period and persists for >6 months. Obtaining an abdominal radiograph in the upright position during the neonatal period is sometimes difficult, depending on the patient's condition. As an exception, confirmation of air fluid levels on radiographs was not necessarily required in the neonatal period.

Fisher's exact test was used for the analysis of categorical data. Student's *t* test was used for the analysis of numerical data. A p value of <0.05 was considered statistically significant. Ekuseru-Toukei 2010 (Social Survey Research Information Co., Ltd., Tokyo) software was used to complete the statistical analysis.

This study was performed in accordance with the *Ethical Guidelines for Clinical Research* published by the Ministry of Health, Labor, and Welfare of Japan on July 30, 2003. This study was approved by the ethical committee for clinical research of Kyushu University Hospital (approval No. 24-163).

2. Results

2.1. Demographic information

A total of 92 responses (43 males, 49 females) were collected from 47 pediatric facilities. The mean age of the patients was 14.4 years (median, 11 years, range, 0–44 years) at the time of the survey.

On the basis of the aforementioned indications and exceptions of the patients in the neonatal period, 62 patients who matched the inclusion criteria for pediatric CIPO were further analyzed (Onset during the neonatal period; n = 35, 1 to 12 months after birth; n = 12, 1 year to <7 years after birth; n = 9, >7 years after birth; n = 6). All the reported disorders were limited to the hollow viscera. Responses on the remaining 30 patients were insufficient to diagnose as CIPO (Fig. 1).

2.2. Clinical features

More than half the patients developed CIPO during the neonatal period (Fig. 2). There were no statistically significant differences in sex (male-to-female ratio; $p = 0.25$) and gestational period (preterm delivery-to-term delivery ratio; $p = 0.62$) between the patients with neonatal onset and those with postneonatal onset. In addition, no statistically significant difference in birth weight distribution was observed between the 2 groups (mean ± SD, 2867.8 ± 794.0 g vs. 2952.8 ± 623.3 g, respectively; $p = 0.67$). Familial accumulation was found for 2 patients. A total of 4 female patients (6.5%) had a familial incidence. Twins, both with megacystis, developed CIPO during the neonatal period, while sisters, both with galactosemia, developed CIPO while school age.

Most of the patients presented with abdominal distension.

The affected lesions were distributed widely throughout the intestinal tracts. Anorectal reflex evaluation (36/62), rectal suction biopsy, and pathological evaluation (36/62) were performed in up to 60% of the patients, followed by contrast enema examination performed in more than 80% (51/62) patients (Table 2).

2.3. Treatments

The patients were treated according to the local protocol of each facility. No treatment modality clearly effective in relieving symptoms.