



Nationwide survey of outcome in patients with extensive aganglionosis in Japan

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Abstract

Purpose Hirschsprung's disease-related short bowel syndrome (HDSBS) is characterized by aganglionosis that extends orally to 75 cm from Treitz's band. The condition is reported to be associated with a high mortality rate of 50–80%. This retrospective study aimed to survey the current trends in HDSBS treatment in Japan.

Methods Patient data were extracted from the results of a nationwide survey we conducted, resulting in the retrospective collection of the data of 1087 HD patients from 2008 to 2012 in Japan.

Results A total of 11 (0.9%) cases of HDSBS were noted. All patients underwent jejunostomy as neonates. Radical procedures performed in five patients (A-colon patch method in four, Duhamel's procedure in one). Ziegler's myotomy-myectomy and serial transverse enteroplasty (STEP) were performed in each patient as palliative procedures. No radical operations were performed in 4 of the 11 cases. The mortality rate was 36.4%. Four patients died, 1 patient who underwent STEP and 3 patients who received no radical procedures. The causes of death were sepsis due to enterocolitis or central intravenous catheter infection, and hepatic failure. All patients who underwent radical procedures survived and showed satisfactory outcomes.

Conclusion HDSBS still showed a high mortality rate, although surgical approaches such as the A-colon patch method resulted in satisfactory outcomes.

Keywords Hirschsprung's disease · Nationwide survey · Short bowel syndrome · Mortality

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Introduction

Recently, the treatment of Hirschsprung's disease (HD) has improved and satisfactory outcomes can be achieved in many cases. However, the management of total colon aganglionosis, especially that with small bowel involvement, remains difficult, and the outcomes are not necessarily satisfactory [1–3]. In our report [4], Hirschsprung's disease-related short bowel syndrome (HDSBS), a condition characterized by aganglionosis extending orally to 75 cm from Treitz's band, was associated with a high mortality rate of 50–80% in Japan. HDSBS differs from standard SBS due to the lack of a colon, and the outcome of HDSBS patients is worse than that of standard SBS patients. This retrospective study aimed to clarify the current outcomes of HDSBS based on the results of a nationwide survey in Japan.

Patients and methods

This retrospective study was performed according to the Ethical Guideline for Clinical Research published by the Ministry of Health, Labour and Welfare of Japan on July 30, 2003 (revised 2008) and complied with the 1964 Declaration of Helsinki (revised in 2008). The study was approved by the clinical research ethics committee of Kyushu University Hospital (No. 27-273 and 28-155). All subjects gave their informed consent prior to their inclusion in this study.

From 2008 to 2012, we sent questionnaires to 156 pediatric surgery departments at major universities and hospitals

throughout Japan. The questionnaires were designed to collect data on the general demographics of patients with HD, as well as their diagnosis, treatment, and outcomes [1]. We received responses concerning 1,087 patients with HD from 156 medical institutions, including 11 (0.9%) patients with HDSBS. We surveyed the general features, surgical management, and outcomes of the 11 patients with HDSBS.

Results

General features

The estimated incidence of HDSBS, which was based on the annual number of cases divided by the annual number of newborns from the annual report provided by the Ministry of Health and Welfare, Japan, was 1/456,412, and the male-to-female ratio was 2.7:1 (Table 1). Patients with a family history of HD accounted for 18.2% of the HDSBS population (Table 1). The incidence of associated anomalies was estimated to be 27.3% (Table 1). Down syndrome was not found among these patients.

Enterostomy

All patients underwent jejunostomy as neonates (Table 2). The average age at the time of jejunostomy was 5 days (median: 2 days).

Table 1 General features of patients with HDSBS compared to total HD during 2008–2012 [1]

	Number of patients	Estimated incidence	Male/female	Familial history (%)	Associated anomalies (%)
HDSBS	11 (0.9%)	1/456,412	2.7:1	18.2	27.3
Total HD [1]	1087	1/4895	2.9:1	7.1	18.9

HDSBS Hirschsprung's disease-related short bowel syndrome, *HD* Hirschsprung's disease

Table 2 Surgical management of patients with HDSBS

Creation of enterostomy	Site of enterostomy	Radical procedures	Redo operation
11/11 (100%)	Jejunum: 11/11 (100%)	7/11 (63.6%) 4: Ascending colon patch method 1: Duhamel 1: Extended myotomy-myectomy (Ziegler's procedure) 1: STEP	3/11 (27.3%) 2: myotomy 1: Extended myotomy-myectomy (Ziegler's procedure)

HDSBS Hirschsprung's disease-related short bowel syndrome, *STEP* serial transverse enteroplasty

Radical procedure

Radical procedures were performed in 5 of the 11 HDSBS cases. Among these, 4 underwent procedures using the ascending colon patch method, and one underwent Duhamel's procedure extending to the sigmoid colon. Two of the 11 cases underwent extended myotomy–myectomy (Ziegler's procedure; $n = 1$) and serial transverse enteroplasty (STEP; $n = 1$) as a palliative radical procedure. The remaining 4 patients did not undergo any radical procedures because it was contraindicated by their condition. Redo operations were performed in three patients (myotomy, $n = 2$; Ziegler's procedure, $n = 1$) (Table 2).

Results of treatment

The mortality rate was 36.4%. Four of the 11 patients with HDSBS died, including 3 patients who did not undergo any radical procedures and 1 who underwent STEP (Table 3). The causes of death were sepsis ($n = 3$) due to enterocolitis or central intravenous catheter infection, and hepatic failure ($n = 2$) after long-term parenteral nutrition. All five patients who underwent radical procedures survived and showed satisfactory outcomes.

Discussions

According to our findings, HDSBS is a rare variant type of HD. The sex ratio of patients with HDSBS was the same as in a previous report [1]. Among the patients with HDSBS, 18.2% had a family history and the incidence of associated anomalies was 27.3%, which was higher in comparison to the overall HD population [1]; however, none of our patients had Down syndrome.

All patients underwent enterostomy in the neonatal period, which meant that the diagnosis of total aganglionosis with small bowel involvement was difficult to differentiate

from congenital hypoganglionosis, immaturity of ganglia, or intestinal atresia.

Standard SBS most often results from a neonatal insult, such as necrotizing enterocolitis, complicated gastroschisis, intestinal atresia, or midgut volvulus. Although SBS is associated with a high mortality rate of up to 37.5% in the first 5 years of life [5], patients with standard SBS often retain their colon [5], which may be why they have an impressive potential for gut adaptation and independence from parenteral nutrition. In contrast, patients with HDSBS often lack a colon, so they may have difficulty achieving gut adaptation, continue to experience diarrhea and malnutrition, and sometimes suffer changes in the gut microbial flora and develop bacterial translocation.

As a definitive operation, many different procedures have been performed for total aganglionosis with small bowel involvement. In our previous report [4], the Martin procedure was the most common surgery; however, the mortality rate was relatively high at 8–12%. On the other hand, the mortality rate among cases in which ascending colon patch procedures are used is low. In our findings, 4 of 11 patients with HDSBS underwent ascending colon patch procedures with satisfactory outcomes. Amerstorfer et al. [6] stated that this procedure has two potential advantages: the preservation of the right colon as an isoperistaltic onlay with its water and electrolyte absorptive capacity as a reservoir between the right colon and ileum, and the preservation of the ileo-cecal valve as a natural barrier to prevent backwash, thereby reducing the incidence of enteritis and associated malabsorption.

Our previous report [1] noted a decrease in the mortality rate for patients with HD, whereas the mortality rate of patients with aganglionosis extending orally to more than 30 cm of the terminal ileum remained high. Importantly, our report showed that HDSBS is still associated with a high mortality rate. In comparison to the results of previous reports [1–4], the mortality rate of patients with HDSBS decreased from 60 to 80–36.4%. Developments in pediatric nutritional support, the diagnosis and treatment, and the selection of ideal radical operations for HDSBS patients may have played roles in the recent decrease in the mortality rate [2, 7]. However, sepsis was the most frequent cause of death, followed by hepatic failure due to long-term parenteral nutrition. HDSBS patients with hepatic failure may be good candidates for small intestine or multivisceral transplantation [8, 9]. Surgical intestinal lengthening procedures, such as STEP and small intestine or multivisceral transplantation, are considered novel therapies for the management of SBS in children [10]. In addition, in recent years, regenerative medicine (stem cell therapy) and tissue engineering have also been considered as treatments for HD [11, 12].

In conclusion, HDSBS still showed a relatively high mortality rate of 36.4%, although surgical approaches such

Table 3 Mortality rate of patients with HDSBS compared to patients with HD during 2008–2012 [1]

	Mortality rate (%)
HDSBS	36.4
Total HD [1]	2.4
Rectum-right colon	0.9
Total colon	4.2
Small intestine	25.0

HDSBS Hirschsprung's disease-related short bowel syndrome, *HD* Hirschsprung's disease, Small intestine, aganglionosis extending orally to more than 30 cm of the terminal ileum

as the ascending colon patch method resulted in satisfactory outcomes. The further development and indications of new treatment strategies for HDSBS, such as small intestine transplantation and regenerative medicine, are yet called for.

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Compliance with ethical standards

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Declaration of Helsinki and its later amendments or comparable ethical standards. All subjects gave their informed consent prior to their inclusion in this study. This retrospective study was also approved by the clinical research ethics committee of Kyushu University Hospital (No. 27-273 and 28-155).

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