ORIGINAL

Is acetylcholinesterase activity in neorectum after laparoscopic endorectal pull-through method for Hirschsprung's disease a primary or a secondary condition?

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Abstract : Between 1996 and 2002, 22 cases of Hirschsprung's disease were treated laparoscopically by endorectal pull-through operation. The proximal margin of the resected bowel materials from these 22 patients were examined histologically by frozen sections at surgery and also after surgery using H&E staining, and complete resection of the aganglionic segment was confirmed. Eleven patients, in whom an informed consent was obtained at randomly, underwent suction biopsy from the pulled-though neorectum after surgery. Of these 11 patients, 2 revealed many AchE-positive nerve fibers in the lamina propria, the muscularis mucosa and around the ganglion cells in the submucosal plexuses. These structural changes were similar to intestinal neuronal dysplasia that was characterized by hyperganglionosis and other neuronal abnormalities. The remaining 9 revealed no AchE activity. Unexpectedly, the two patients showing AchE activity in their neorectum continued to have persistent constipation and were treated with laxatives or glycerin enema. It was suggested that their persistent constipation was caused by intestinal neuronal dysplasia showing an abnormal increase of AchE activity in spite of presence of ganglion cells of the neorectum after surgery, but it was uncertain that they were primary condition as a HaIND or secondary reactions after surgery. J. Med. Invest. 53 : 113-116, February, 2006

Keywords **:** *Hirschsprung's disease, intestinal neuronal dysplasia (IND), HaIND acetylcholinesterase, constipation, endorectal pull-through operation*

INTRODUCTION

It is known that some patients with Hirschsprung's disease continue to have persistent bowel dysfunction after definitive surgery in spite of complete resection of the aganglionic bowel segment. The postoperative bowel dysfunction revealed entelocolitis (6% to 20%) (1-3), constipation and soiling (11% to 35%)(4-7). Since in 1973 Lassmann and Wurnig were the first describe two patients with hyperganglionosis of the proximal segment to the aganglionic bowel (8), that was later called intestinal neuronal dysplasia (IND) and similar to symptom of Hirschsprung's disease, some investigators have reported subsequently that 25% to 40% of patients with Hirschsprung's disease had associated IND (HaIND) (9-16). Therefore, it is suggested that the postoperative persistent constipation of Hirschsprung's disease is caused by HaIND (13, 15). This study describes 2 patients with HaIND, who had persistent constipation after endorectal pull-through operation for Hirschsprung's disease.

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MATERIALS AND METHODS

Between 1996 and 2002, one experienced pediatric

surgeon at the Tokushima University Hospital carried out laparoscopic endorectal pull-through operation (17) in 22 patients with Hirschsprung's disease, 14 boys and 8 girls ranging in age from 14 days to 10 years. Of these 22 patients, 20 were treated with primary endorectal pull-through procedure laparoscopically, and the remaining 2 were transferred from other hospital after construction of colostomy and also treated with secondary endorectal pull-through procedure laparoscopically. The proximal margin of the resected bowel materials from these 22 patients were examined histologically by frozen sections at surgery and also after surgery using H&E staining, and complete resection of the aganglionic segment was confirmed. Eleven patients ranging from 3 months to 6 years after surgery, in whom an informed consent was obtained at randomly, underwent suction biopsy from the pulled-though neorectum. These biopsy specimens were demonstrated histochemically for AchE activity by Karnovsky & Roots method (18). The evaluation for AchE activity was referred to Kobayashi's classification (19).

RESULTS

Of these 11 patients, four complained postoperative bowel problems. Three patients including one with 21-trisomy continued to have persistent constipation, and one that was pulled-through with the ceacum revealed enterocolitis after definitive surgery (Table 1). Two of 3 patients with persistent constipation revealed many AchE-positive nerve fibers in the lamina propria, the muscularis mucosa and around the ganglion cells in the submucosal plexuses (Fig.1, 2). These structural changes were similar to intestinal neuronal dysplasia that was characterized by hyperganglionosis and other neuronal abnormalities. The remaining 9 revealed no AchE activity and normal ganglion cells in the submucosal plexuses.

DISCUSSION

Intestinal neuronal dysplasia that was described as a pseudo-Hirschsprung disorder by Meier-Ruge

Table 1. CASES WITH SUCTION BIOPSY FROM THE NEORECTUM AFTER SURGERY

	sex	Age at Surgery	Extent of Aganglionosis	colostomy	Surgery	Biopsy after Surgery	Enterocolitis	Constipation	Activity of AchE	Notes
1	m	30-d	rectosigmoid	(−)	lap.S	3-yr	(−)	(+)	(+)	
2	m	62-d	sigmoid	(−)	lap.S	6-mo	(−)	(+)	(+)	
3	m	22-d	rectum	(−)	lap.S	1.5-yr	(−)	(+)	(−)	21-trisomy
4	m	70-d	rectosigmoid	(−)	lap.S	1.6-yr	(−)	(−)	(−)	
5	f	6-yr	rectosigmoid	(−)	lap.S	2-yr	(−)	(−)	(−)	
6	f	2-yr	rectum	(−)	lap.S	3-mo	(−)	(−)	(−)	
7	f	46-d	rectum	(−)	lap.S	5-yr	(−)	(−)	(−)	
8	m	6-mo	rectum	(−)	lap.S	1.4-yr	(−)	(−)	(−)	
9	m	43-d	sigmoid	(+)	lap.S	6-yr	(−)	(−)	(−)	
10	m	9-mo	transvers	(+)	lap.S	5-yr	(+)	(−)	(−)	
11	f	2-yr	rectum	(−)	lap.S	6-mo	(−)	(−)	(−)	

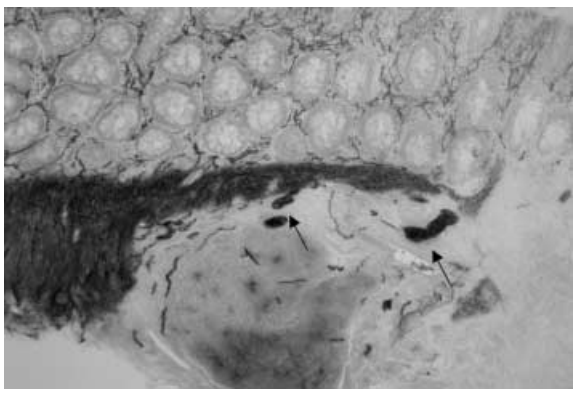

Figure 1: Case 1: acethylcholinesterase (AchE) staining: many AchE positive fibers in lamina propria, muscularis mucosae and submucosal layer with large plexuses (arrows)(original magnification ×100)

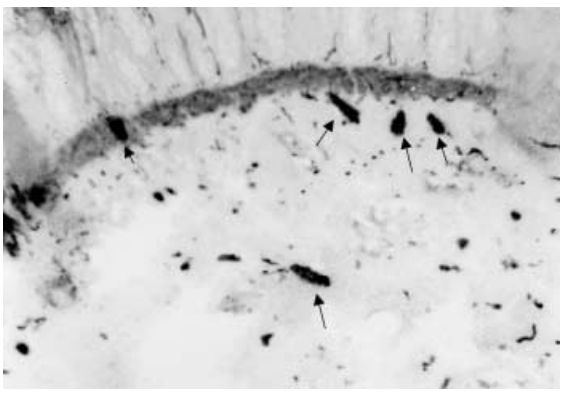

Fig 2: Case 2: acethylcholinesterase (AchE) staining: moderate numbers of AchE positive fibers in lamina propria, muscularis mucosae, many submucosal plexuses (arrows) and heterotopic plexus (small arrow). (original magnification ×100)

in 1971 (24) was characterized by structural changes consisting of hyperplasia of the submucosal and myenteric plexus with formation of giant ganglia, moderate increase in the number of AchE positive nerves in the lamina propria, and circular muscle and presence of isolated ganglion cells in the lamina propria. Two years later, Lassmann and Wurnig (8) reported the first description of two patients with hyper-ganglionosis of the proximal segment to the aganglionic bowel. Some investigators have reported consecutively that 25% to 40% of patients with Hirschsprung's disease had associated IND(HaIND) (9-16). Therefore, it is suggested that the postoperative persistent bowel dysfunction of Hirschsprung's disease is caused by HaIND (13, 15), because an increase in intestinal cholinergic activity may increase gut contraction that leads to disturbance of gut motility (19). On the other hand, however, some investigators reported that it was unknown whether abnormal increase of AchE activity in spite of presence of ganglion cells in HaIND is a primary or a secondary condition. In inflammatory bowel diseases such as ulcerative colitis or Crohn's disease, reactive ganglion cell hyperplasia and hypertrophy as well as a widening of and an increase in the neurofilaments have been described (20-23). In our past clinical series, some cases complained constipation treated by Duhamel-Ikeda's procedure had not revealed AchE activity in the neorectum such as this series. It was also suggested that AchE activity in the neorectum after surgery might depend on differences between Duhamel-Ikeda's procedure and endorectal pull-through method.

In order to avoid the postoperative persistent bowel dysfunction, it is necessary to have an assessment of the colon innervation with serial biopsies of the proximal segment of the aganglionic zone before surgery for Hirschsrung's disease (25, 26). As our two cases had not serial biopsies of them before or at surgery, it was difficult to detect that they were HaIND or not. A surgical management of HaIND is controversial and there are no reports about long-term results. Hanimann et al (15) suggested that HaIND might be a distinct disease compared to isolated IND with all its well-known complication and that HaIND dose not influence the long-term outcome in patients with Hirschsprung's disease, and the neuronal dysplastic segment may be retained without increased risks or morbidity. Fadda et al (11) suggested that a resection of IND segments was often unnecessary because colon motility in IND tended to normalize within the first 3 years of life. On the other hand, some investigators suggest that co-existing neuronal dysplastic segment above aganglionosis should be considered secondary resection under histomorphologic mapping because of a possible cause of persistent bowel symptoms after pull-through operation for Hirschsprung's disease (13, 15, 19).

Unexpectedly, our two patients excluding one with 21-trisomy showed abnormal increase of AchE activity in their neorectum after surgery and they continued to have persistent constipation and were well-controlled with laxatives or glycerin enema. Although there are some questions and issues in HaIND or not, longer follow-up is necessary to access the outcome in our patients.

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