รายงานผู้ป่วย

# Chronic idiopathic intestinal pseudoobstruction in children: a report of two cases

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*Cases of two children with the diagnosis of chronic idiopathic intestinal pseudoobstruction are presented. The clinical course was characterized by intermittent episodes of abdominal distension, constipation and malnutrition. Diagnosis was based on typical symptoms and the absence of mechanical obstruction upon exploratory laparotomy. In both patients, the large intestine and rectal biopsies contained ganglion cells. Treatment was directed at relieving symptoms, which in one patient became persistent and required total parenteral nutrition.*

**Key words** : *Chronic idiopathic intestinal pseudoobstruction, Children.*

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**วรนุช จงศรีสวัสดิ์, บุษบา วิวัฒน์เวคิน, พงษ์พีระ สุวรรณกูล. รายงานผู้ป่วยเด็กโรคลำไส้โป่งพองเรื้อรังโดยไม่ทราบสาเหตุจำนวน 2 ราย. จุฬาลงกรณ์เวชสาร 2540 ม.ค;41(1): 61-71**

*ผู้ศึกษารายงานผู้ป่วยเด็กโรคลำไส้โป่งพองเรื้อรังโดยไม่ทราบสาเหตุจำนวน 2 ราย ลักษณะอาการทางคลินิกมีอาการท้องอืดเป็น ๆ หาย ๆ ท้องผูก และขาดสารอาหาร การวินิจฉัยอาศัยจากอาการที่มีลักษณะเฉพาะ และไม่พบการอุดตันของลำไส้จากการผ่าตัดผู้ป่วยทั้งสองรายมี ganglion cells ในลำไส้ใหญ่ และ rectum การรักษาเป็นการรักษาประคับประคอง และให้สารอาหารให้เพียงพอ ซึ่งในผู้ป่วยรายหนึ่งจำเป็นต้องได้รับอาหารทางหลอดเลือดตลอดเวลา*

Chronic idiopathic intestinal pseudoobstruction (CIIP) is a clinical syndrome characterized by signs of intestinal obstruction without demonstrable occlusion of the gut and in the absence of a recognized underlying disease.[1] It belongs to the loosely defined group of functional disorders of GI motility.[2] GI motility is physiologically controlled by the interaction of three factors: the electrical activity of the smooth muscle cells, the intrinsic and extrinsic nerves and the neuropeptide system.[3] Therefore, an abnormality of any one of these factors theoretically can cause severe gastrointestinal motility disturbance and intestinal pseudoobstruction. There have been reports of patients with severe abnormal gastrointestinal motility caused by either smooth muscle dysfunction or autonomic nerve dysfunction (intrinsic or extrinsic nerves) of the gastrointestinal tract[4,5] but not from gastrointestinal hormonal disturbance. Conditions associated with secondary pseudoobstruction in adults (Table 1) are not common in pediatric patients.[6-8]

**Table 1.** Conditions associated with secondary chronic intestinal pseudoobstruction.[9]

| | |
|---|---|
| A. Diseases involving smooth muscle | |
| Collagen-vascular disease | Scleroderma, Dermatomyositis/polymyositis, Systemic lupus erythematosus, Periarteritis nodosa |
| Amyloidosis | |
| Primary muscle disease | Myotonic dystrophy, Progressive muscular dystrophy |
| B. Endocrine disorders | Hypothyroidism, Hypoparathyroidism, Diabetes mellitus, Pheochromocytoma |
| C. Neurologic diseases | Parkinson's disease, Hirschsprung's disease, Intestinal hypoganglionosis, Chagas' disease, Familial autonomic dysfunction, Spinal cord injury, Pseudo-Hirschsprung's disease, Multiple sclerosis, Ganglioneuroma of the intestine. |
| D. Drug associated | Tricyclic antidepressants, Antiparkinsonian drugs, Ganglionic blockers, Phenothiazines, Clonidine, Opiates, Verapamil, Vincristine. |
| E. Miscellaneous | Celiac disease, Jejunoileal bypass, Mesenteric vascular insufficiency, Ceroidosis, Radiation enteritis, Alcoholism, Psychosis, Cathartic colon, Lung cancer, Neoplasm with or without celiac plexus invasion, Malrotation, Strongyloides infection, Cytomegalovirus infection, Human immunodeficiency virus infection, Neurofibromatosis, Azotemia, Porphyria, Amanita mushroom poisoning, Lead poisoning, Diffuse lymphoid infiltration. |

This paper reports two cases of CIIP in which the clinical manifestations, and radiological and histopathological techniques were employed in the diagnosis.

## Case Reports

### Case 1

W.C., a Thai girl of 3,950 grams birth weight was the only child of unrelated parents without a family history of intestinal obstruction. She developed abdominal distension, constipation and vomiting at the age of 1 month. At 7 months of age, she was referred to Chulalongkorn University Medical School with a diagnosis of Hirschsprung's disease by barium enema which demonstrated dilatation of the colon and rectum. She had been operated on twice by the referring physician due to apparent intestinal obstruction that had not been relieved by conservative treatment. At exploratory laparotomy, the colon and rectum were dilated without mechanical obstruction, so a sigmoid colostomy was performed.

Physical examination at the age of 7 months showed a malnourished girl, 5,000 grams weight, with abdominal distension and decreased bowel sounds. Her laboratory studies showed Hb 13.4 gm/dl, white blood cell count 8,200 per cu. mm. (PMN 33%, monocyte 14%, lymphocyte 53%), and platelet count 500,000 per cu. mm. Serum electrolyte revealed $Na^+$ 140 mEq/L, $K^+$ 4.7 mEq/L, $Cl^-$ 107 mEq/L, $CO_2$ 19 mEq/L. She had been operated three times at our hospital because of recurrent intestinal obstruction and prolapsed colostomy but no evidence of mechanical obstruction was ever found. The last operative finding showed a paper-thin bowel wall from the duodenum to the ileocecal valve, and a dilated and thin-wall large intestine. Due to perforation at jejunum, a small bowel resection with end-to-end anastomosis and a revised colostomy were done. The histopathology of the proximal jejunum, colon and rectum demonstrated hypertrophy of muscular layers and degeneration of ganglion cells (Figure 1). Nutrition was maintained mainly by total parenteral nutrition. Multiple pharmacological agents, including cisapride and domperidone, failed to induce proper peristalsis. She also developed recurrent urinary tract infection. The intravenous pyelogram showed enlarged pelvicalyceal systems, dilated and tortuous ureters with an enlarged urinary bladder (Figure 2). She died at the age of 2 years from catheter related sepsis. Autopsy permission was not granted.

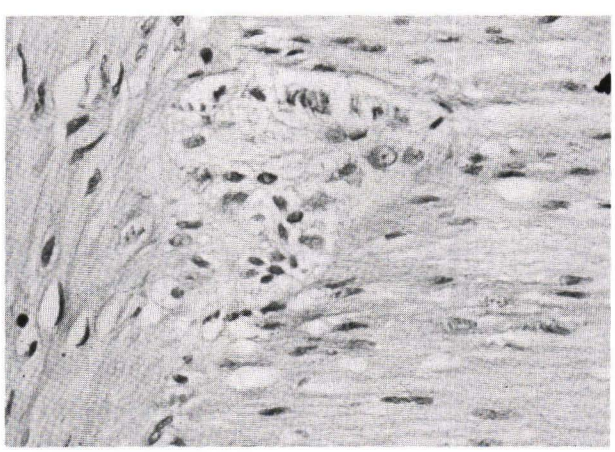

**Figure 1.** Proximal jejunum showed degeneration of ganglion cells.

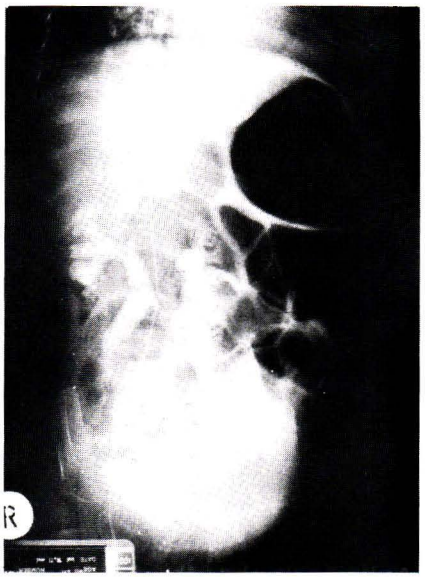

**Figure 2.** The intravenous pyelogram showed hydroureters and hydronephrosis.

### Case 2

C.K., a Thai boy had developed abdominal distension, constipation and loss of body weight at age 4 years. He was the third child of unrelated parents without a family history of intestinal obstruction.

Physical examination showed a pale, cachectic boy of 11 kgs weight. He had marked abdominal distension and normal bowel sounds. His laboratory studies showed Hb 9 gm/dl with hypochromic and microcytic morphology, white blood cell count 6,300 per cu. mm. (PMN 39%, monocyte 10%, lymphocyte 51%), and platelets 454,000 per cu. mm. Liver function tests were normal. The serum B-carotene was 80 ug/dl (normal = 60-300 ug/dl). The D-Xylose test showed mildly decreased serum level to 22 mg/dl (normal > 25 mg/dl). Bacterial overgrowth was documented by recovering fluid from his proximal intestine, which was positive cultured for alpha streptococcus. Findings on upper gastrointestinal barium study included delayed gastric emptying and dilated loops of the large intestine.

At exploratory laparotomy, the whole colon was dilated, but was absent of peristalsis and without mechanical obstruction. A right-sided transverse colostomy was done. Histological examination of the rectum showed hypertrophy of muscular layers with fibrosis. Over the next 3 years the patient easily tolerated enteral nutrition and had a 6 kilogram weight gain. No repeated hospitalization for parenteral nutrition and pharmacological treatment were needed. After that, he was lost to follow-up.

## Discussion

Chronic intestinal pseudoobstruction (CIIP) is a disorder of gut motility that may result from a number of different underlying conditions.[10] It can be divided into two types: (a) primary or idiopathic and (b) secondary types. CIIP was first described by Dudley et al in 1958.[11] Several cases of pseudoobstructive syndromes have been reported in the literature, frequently under different names such as pseudo-Hirschsprung, hypoganglionosis, chronic adynamic ileus, adynamic bowel syndrome, colonic neuronal dysplasia and megacystis-microcolon-intestinal hypoperistalsis syndrome.[12-15]

CIIP can occur in patients of all ages. A national survey of CIIP in pediatrics was reported

by Vargas et al.[6] They identified 87 cases of CIIP from 25 centers. The clinical manifestations included abdominal distension (85%), constipation (60%), vomiting (59%), failure to gain weight (27%), diarrhea (25%), failure to void (18%), urinary tract infection (13%), seizures (6%), temperature instability, blood pressure instability and dysphagia. Radiographic studies showed gastroesophageal reflux (52%), delayed gastric emptying (26%), megaduodenum (24%), generalized dilatation of the small intestine (36%), delayed transit through the small intestine (12%), segmentation of the barium and microcolon (10%) or partial malrotation (12%).

CIIP syndromes have been histopathologically classified into three types: (a) myopathic, (b) neuropathic, and (c) no recognizable neuropathy or myopathy.[5] Pathologic findings of full-thickness biopsies of the gastrointestinal tract in visceral myopathy may be degeneration and vacuolization of muscular layers. A Masson-trichrome technique may reveal collagen deposition. In visceral neuropathy, when specific silver stains are used according to the Smith technique, it may show abnormality of the neurons and axons. CIIP can also be divided into two types: (a) the familial and (b) the nonfamilial or sporadic types.[16]

Familial visceral myopathies are characterized by degeneration and fibrous replacement of smooth muscle of the gastrointestinal tract and, in some cases, the urinary tract.[6] Five types of familial visceral myopathy have been identified as shown in Table 2.[9]

Visceral neuropathies consist of two forms characterized by degeneration of the myenteric plexus. One form is familial, which may involve the central and peripheral nervous systems as well as the intestinal nervous system. Five different types of familial visceral neuropathy have been reported (Table 3).[9] The other form, called sporadic visceral neuropathy, involves degeneration of the intestinal nervous system without the intranuclear inclusions. There are no distinctive gastrointestinal clinical features even when compared with visceral myopathies.

Stanghellini et al reported four major patterns of intestinal manometric abnormality in CIIP.[17] They included (a) aberrant propagation and/or configuration of interdigestive migrating motor complexes or MMC. Two major abnormalities occur in this category. One, absence of propagation of phase III activity (either simultaneous or retrograde) over at least a 30 cm. segment of small bowel. Two, marked tonic (> 30 mmHg amplitude; > 3 min duration) rises of baseline pressure during propagation of the activity front through one or more levels of the small bowel assessed. (b) Bursts of non-propagated phasic pressure activity in the fasting and fed states. Bursts were defined as periods of at least two minutes duration with continuous high amplitude (> 20 mmHg) and high frequency (10-12/min) phasic pressure activity that were not propagated and not followed by motor quiescence (in contrast to typical phase III activity of the MMC). (c) Sustained (for over 30 min) and intense phasic

**Table 2.** Findings in 5 reported families with visceral myopathy.

| Type | Genetic Transmission | Gastrointestinal Lesions | Extraintestinal Lesions |
|---|---|---|---|
| Type I | Autosomal dominant | Dilated proximal gut, including esophagus and duodenum; redundant colon | Megacystis |
| Type II | Autosomal recessive | Dilated gastric and small bowel (slight); intestinal diverticulum | External ophthalmoplegia, ptosis, no bladder involvement |
| Type III | Autosomal recessive | Gastroparesis; narrowed tubular, small bowel; normal esophagus and colon | None observed |
| Type IV | Autosomal recessive | Dilated entire gut | None observed |
| Type V | | Megaduodenum | Basal cell carcinoma, megacystis |

**Table 3.** Findings in 5 reported families with visceral neuropathy.

| Type | Genetic Transmission | Gastrointestinal Lesions | Microscopic Lesions | Extraintestinal Lesions |
|---|---|---|---|---|
| Type I | Autosomal recessive | Megaduodenum; generalized dilatation of small intestine; redundant colon | Atrophy of longitudinal muscle layer in all gastrointestinal tissue; degenerative changes in argyrophobic myenteric plexus neurons | Mental retardation; ataxia, autonomic dysfunction, dysarthria, absent deep tendon reflexes, sensory neuropathy |
| Type II | Autosomal recessive | Dilatation and nonperistaltic hyperactivity of esophagus, stomach,and small intestine; extensive colonic diverticulosis | Reduction and degeneration of myenteric plexus neurons; intra-nuclear inclusions in myenteric and submucosal plexus neurons | No mental retardation; ataxia, autonomic deep tendon reflexes, sensory neuropathy |
| Tyep III | Autosomal dominant | Delayed gastric emptying; generalized dilatation of small intestine | Hypertrophy of smooth muscle; hyperplastic and degenerative changes of argyrophilic neurons and axons in the myenteric plexus | None observed |
| Type IV | Autosomal dominant | Abnormal gastric emptying; segmental dilatation of jejunum and ileum | Hypertrophy of smooth muscle; reduction and degeneration of myenteric plexus argyrophilic neurons | None observed |
| Type V | Autosomal recessive | Abnormal gastric emptying; dilated stomach and duodenum; nondilated jejunum and ileum | Limited tissue; normal smooth muscle; neural fibers in muscle layer hypertrophied; no ganglion cells | External ophthalmoplegia, peripheral neuropathy, neuronal hearing loss; no retardation |

pressure activity that occurred in a segment of intestine while normal or reduced activity were noted simultaneously at other levels of the intestine. (d) Inability of the ingested meal to change fasting intestinal activity into a fed pattern.

Prolonged (6-24 hr) manometric recordings from the stomach and small bowel helped to define better the diagnosis and to differentiate among mechanical bowel obstruction, visceral myopathies and visceral neuropathies.[18] When present, repeated clusters of phasic and tonic pressure activity, especially after a test meal, are indicative of a mechanical obstruction. In visceral myopathies, the phasic pressure waves of the MMC are of low amplitude or absent. In visceral neuropathies, the pressure waves are present, but uncoordinated.

Schuffler et al demonstrated abnormalities of esophageal motility in 5 patients with CIIP.[19] The primary peristalsis was absent or replaced by simultaneous contractions and repetitive spontaneous activity and the lower esophageal sphincter failed to relax. Anal manometry revealed the presence of a recto-anal inhibitory reflex, excluding the possibility of Hirschsprung's disease.

Devane et al suggested that the non-invasive technique of surface electrogastrography might provide a useful screening test of the pathophysiological basis of the functional obstruction in children with CIIP.[20] Abnormalities were present in 8 of 11 patients including persistent tachygastria (electrical control activity frequency > 5 cycles/minute) and continuously irregular frequency.

The principal methods of management of CIIP are correction of dehydration, electrolyte replacement, nutritional balancing, prokinetic agents, suppression of bacterial overgrowth, decompression and consideration of surgical treatment.[21] Treatment is unsatisfactory in most, like our patient case 1, because, until recently, no medication has been effective in improving motility and, in many, the medications fail to be transported and absorbed effectively.

In conclusion, we can now diagnose CIIP with no need to perform an exploratory laparotomy by using the clinical manifestations, the radiologic findings, electrogastrography and motility studies of the gastrointestinal tract.

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