Pediatrics & Therapeutics

Muto et al., Pediat Therapeut 2015, 5:1
http://dx.doi.org/10.4172/2161-0665.1000236

Research Article Open Access

Data Mined Distinctive Features of Pediatric Chronic Idiopathic Intestinal Pseudo-obstruction in Japan

Mitsuru Muto[1*], Hiroshi Matsufuji[1], Fuminori Muranaga[2], Takeshi Tomomasa[3], Atsushi Nakajima[4] and Tomoaki Taguchi[5]

[1]*Department of Pediatric Surgery, Developmental Medicine, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan*

[2]*Department of Medical Informatics, Human and Environmental Sciences, Kagoshima University Graduate School of Medical and Dental Sciences, Kagoshima, Japan*

[3]*PAL Children's Clinic, Isesaki, Gunma, Japan*

[4]*Division of Gastroenterology, Yokohama City University School of Medicine, Yokohama, Japan*

[5]*Department of Pediatric Surgery, Reproductive and Developmental Medicine, Graduate School of Medical Sciences, Kyushu University, Fukuoka, Japan*

[*]**Corresponding author:** Mitsuru Muto, Department of Pediatric Surgery, Kagoshima University, 8-35-1 Sakuragaoka, Kagoshima, 890-8520, Japan, Tel: +81 99 275 5444; Fax: +81 99 275 2628; E-mail: mitsuru@m3.kufm.kagoshima-u.ac.jp

Rec date: Feb 04, 2015, **Acc date:** Mar 05, 2015, **Pub date:** Mar 09, 2015

Abstract

Background: A former nationwide survey in Japan on pediatric chronic intestinal pseudo-obstruction (CIPO) determined the most common etiology to be 'idiopathic'. However, currently no appropriate diagnostic criteria for pediatric chronic idiopathic intestinal pseudo-obstruction (CIIP) in children has been defined. The report utilized data mining to identify key clinical features that would qualify statistically CIIP diagnostic criteria.

Methods: Sixty-nine cases were reviewed and subject to standard mining association rule. Cases were assigned to three groups: fully dependent on parenteral nutrition (PN) (group A, n = 15), on partial PN or independent from PN, but requiring permanent enterostomy for decompression (group B, n = 37), and all the other (group C, n = 17). Distinctive features related to each group assignment were then extracted from 87 reported clinical features of the CIPO. The statistical operation was performed by an expert in medical informatics using apriori algorithm.

Results: Key features of patients in group A and B, thought to be severely intractable cases, were the presence of abdominal distension, intestinal dysmotility, ileus without mechanical obstruction, and the absence of histopathological abnormalities in the intramural ganglion cells.

Conclusions: The presence of clinical features of a functional ileus, in the absence of proven histopathological abnormalities, can be used for diagnostic criteria for CIIP covering all the intractable cases in Japanese children. It is highly significant that a normal full-thickness histopathological finding was statistically extracted as one key feature for CIIP in our analysis.

Keywords: Chronic intestinal pseudo-obstruction; Idiopathic; Association rule mining; Histopathological examination

Introduction

Chronic intestinal pseudo-obstruction (CIPO) is characterized by repetitive or continuous episodes of functional ileus [1]. Previously, a nationwide survey was conducted to assess the status of CIPO in Japanese children. The estimated pediatric CIPO prevalence was 3.7 in 1 million children younger than 15 years old. Two-thirds had difficulty on taking ordinary oral diet and nearly half of the patients were dependent on parenteral nutrition (PN). More than half required intestinal decompression with permanent enterostomas. These findings were deemed likely to significantly impact patient quality of life (QOL). Furthermore, only 4.8% children in our review died from enteritis or sepsis. Prognosis with respect to survival was good. We recognized that the number of patients transitioning from childhood to adulthood will increase [2].

CIPO is considered 'idiopathic' when conventional histological examination, such as hematoxylin and eosin staining, failed to show meaningful pathology [1,3]. In our series, most of Japanese children with CIPO exhibited no abnormalities in the ganglion plexus of the affected intestine and was retrospectively considered to be 'idiopathic' [2]. However, an appropriate diagnostic criteria for pediatric chronic idiopathic intestinal pseudo-obstruction (CIIP) is not available and, given the serious long term implications highlighted above, will be beneficial in Japan. We intended to sue statistical techniques to acquire candidate features for diagnostic criteria of CIIP covering all severe and intractable cases based on the former nationwide survey. We used a method of data association mining [4], which has been applied widely in the field of marketing. More recently this approach has been applied to the medical sciences to discover distinctive features that correlate with clinical outcomes using large datasets [5-9]. The aim of this paper is to reveal the data mined distinctive features of CIIP pediatric patients in Japan.

Materials and Methods

Among the 92 cases from 47 Japanese pediatric facilities [2], 69 cases were statistically reviewed. The remainders were excluded due to insufficient data. The data was obtained and the results published based on a survey questionnaire (Table 1) sent to facilities that

included faculty members of the Japanese Society of Pediatric Surgeons; the Japanese Society of Pediatric Nutrition, Gastroenterology, and Hepatology; and the Japanese Study Group of Pediatric Constipation. Severe and intractable cases were considered to be fully depended on PN and/or required continuous intestinal decompression, as expert's opinion in our study group. These factors were most likely to restrict children's QOL. Hence, we sort to define the distinctive clinical features associated with those factors statistically using published rules of data association mining [4].

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
Clinical data considered as the bases for diagnostic judgment (Multiple answers allowed)	□ Onset during the neonatal period □ Onset after the neonatal period □ Repetitive episodes of remission and exacerbation of symptoms □ Onset during the neonatal period and the symptom persists for the first 2 months of life

	□ Onset after the neonatal period and the symptom persists for >6 months □ No sex difference □ Presence of intestinal dysmotility, intestinal obstruction, and functional ileus □ Presence of intestinal dysmotility, intestinal obstruction, and functional ileus □ Presence of highly dilated bowel □ Radiographic documentation of air fluid levels □ Without microcolon □ Gastrointestinal tract widely affected □ Laparotomy findings (presence or absence of peristalsis, and caliber change) □ Colonic inertia □ No histopathological abnormalities in the intramural ganglion cells □ Histologically normal nerve plexuses and smooth muscles on hematoxylin-eosin staining □ No pathological abnormalities in a searchable range □ Pathologically abnormal with smooth muscle fibrosis in muscularis propria □ Abnormalities on gastrointestinal tract manometry □ Peristaltic failure in the gastrointestinal series □ Positive anorectal reflection (Including atypically positive) □ Presence of ganglion cells and absence of hypertrophic AchE-positive nerve fibers in mucosa with suction biopsy □ Without megacystis □ Abnormalities in the urinary tract including megacystis and presence of a voiding disorder □ No consideration of the existence of urination trouble □ Presence of duodenogastric reflux with cine-magnetic resonance imaging
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
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:)
Mild liver function disorder; (1.0 Total bilirubin (mg/dL) 3.0, or 30 ALT (IU/L) 100), Moderate liver function disorder; (3.0 Total bilirubin (mg/dL) 10.0, or 100ALT (IU/L) 300), Severe liver function disorder; (10.0 Total bilirubin (mg/dL), or 300 ALT (IU/L) 100). AchE, acetylcholinestrase.	

Table 1: Questionnaires in the nationwide survey.

All the 69 cases were divided into 3 groups: group A (n=15, 21.7%) fully dependent on PN; group B (n=37, 53.6%) that could live under partial PN support or oral feedings, however requiring permanent enterostoma for decompression; and the remainder, group C (n=17, 24.7%) (Table 2).

Subsequently, 87 clinical terms asked in the questionnaire were obtained. All possible patterns of combinations with these 87 clinical features were created mechanically by using software. Then the frequency and reliability of each potential combination for each group was explored statistically. There are two key indicators subject to statistical analysis: the support value which measures frequency of appearance, and confidence value which measures reliability. For any given combination of clinical features X in group Y, support value is calculated as follows:

Support = number of cases in group Y with clinical features X/total number of cases in the analysis

A higher numerical value for support demonstrates a greater frequency of which the clinical features X are observed in group Y. The confidence value is calculated as follows:

Confidence = number of cases in group Y with clinical features X/ total number of cases with clinical features X

A confidence value closer to 1 is indicative of a stronger relationship between clinical features X and group Y.

Note that this technique is not intended to indicate statistical significance, in the purest sense. The method will only identify the clinical features which have closest relationship to each group. We also mentioned lift value, indicator of statistical independency in referred relationships. Lift value is defined as follows:

Lift = (number of cases in group Y with clinical features X x total number of cases in the analysis)/(number of cases with clinical features X x total number of cases in group Y).

When the lift value is less than 1.0, the relationship between features X and group Y can be said to occur by chance alone and hence are not statistically reliable.

Fully dependent on PN	**Fully dependent on PN (n=15, 21.7%)**	**Requiring partial PN (n=28, 40.6%)**	**Independent from PN (n=26, 37.7%)**
Requiring permanent stoma (n=46, 66.7%)	Group A (n=9, 13.0%)	Group B (n=23, 33.3%)	Group B (n=14, 20.3%)
Unrequiring stoma (n=23, 33.3%)	Group A (n=6, 8.7%)	Group C (n=5, 7.3%)	Group C (n=12, 17.4%)
Dependency on parenteral nutrition and requirement of permanent stoma for decompression were positioned to be factors which restrict patient's quality of daily life. Then all the reviewed cases were assorted into 3 groups upon these factors. PN, parenteral nutrition.			

Table 2: Assortment of reviewed 69 cases.

All the statistical analyses were completed by software, R version 2.15.3 (Security Blanket) for Windows using apriori algorithm, an efficient algorithm for finding all frequent itemsets [10]. After apriori analysis, we sorted results obtained as confidence = 1 in the order that had high support level. All the operations and appropriate statistical judgments were carried out by an expert in medical informatics and statistical analysis in the field of clinical medicine (F.M).

clinical features X	=> group Y	*support*	*confidence*
TPN, Without familial history, Parenteral nutrition, Intestinal dysmotility・Intestinal obstruction・Functional ileus	=>cluster: group A	0.1195652	1
TPN, Without familial history, Without mechanical obstruction, Intestinal dysmotility・Intestinal obstruction・Functional ileus	=>cluster: group A	0.1195652	1
TPN, Without mechanical obstruction	=>cluster: group A	0.1195652	1
TPN	=>cluster: group A	0.1195652	1
TPN, Without familial history, Without mechanical obstruction	=>cluster: group A	0.1195652	1
TPN, Without mechanical obstruction, Parenteral nutrition	=>cluster: group A	0.1195652	1
TPN, Intestinal dysmotility・Intestinal obstruction・Functional ileus	=>cluster: group A	0.1195652	1
TPN, Without familial history, Without mechanical obstruction, Parenteral nutrition	=>cluster: group A	0.1195652	1
TPN, Without familial history, Intestinal dysmotility・Intestinal obstruction・Functional ileus	=>cluster: group A	0.1195652	1
TPN, Without familial history, Without mechanical obstruction, Parenteral nutrition, Intestinal dysmotility・Intestinal obstruction・Functional ileus	=>cluster: group A	0.1195652	1
TPN, Without mechanical obstruction, Intestinal dysmotility・Intestinal obstruction・Functional ileus	=>cluster: group A	0.1195652	1
TPN, Parenteral nutrition	=>cluster: group A	0.1195652	1
TPN, Without familial history	=>cluster: group A	0.1195652	1
TPN, Without mechanical obstruction, Parenteral nutrition, Intestinal dysmotility・Intestinal obstruction・Functional ileus	=>cluster: group A	0.1195652	1
TPN, Parenteral nutrition, Intestinal dysmotility・Intestinal obstruction・Functional ileus	=>cluster: group A	0.1195652	1
TPN, Without familial history, Parenteral nutrition	=>cluster: group A	0.1195652	1
TPN, Without mechanical obstruction, Parenteral nutrition, Intestinal dysmotility・Intestinal obstruction・Functional ileus	=>cluster: group A	0.1086957	1
TPN, Without familial history, Intestinal dysmotility・Intestinal obstruction・Functional ileus	=>cluster: group A	0.1086957	1
TPN, Without familial history, Without mechanical obstruction, Parenteral nutrition, Abdominal distension	=>cluster: group A	0.1086957	1
TPN, Without familial history, Parenteral nutrition, Abdominal distension	=>cluster: group A	0.1086957	1
TPN, Without familial history, Without mechanical obstruction, Abdominal distension	=>cluster: group A	0.1086957	1
TPN, Parenteral nutrition, Intestinal dysmotility・Intestinal obstruction・Functional ileus	=>cluster: group A	0.1086957	1
TPN, Without mechanical obstruction, Intestinal dysmotility・Intestinal obstruction・Functional ileus	=>cluster: group A	0.1086957	1
TPN, Without mechanical obstruction, Parenteral nutrition, Abdominal distension	=>cluster: group A	0.1086957	1
TPN, Without mechanical obstruction, Abdominal distension	=>cluster: group A	0.1086957	1
TPN, Without familial history, Without mechanical obstruction, Parenteral nutrition, Intestinal dysmotility・Intestinal obstruction・Functional ileus	=>cluster: group A	0.1086957	1
TPN, Abdominal distension	=>cluster: group A	0.1086957	1
TPN, Without familial history, Parenteral nutrition, Intestinal dysmotility・Intestinal obstruction・Functional ileus	=>cluster: group A	0.1086957	1
TPN, Without familial history, Without mechanical obstruction, Intestinal dysmotility・Intestinal obstruction・Functional ileus	=>cluster: group A	0.1086957	1
TPN, Intestinal dysmotility・Intestinal obstruction・Functional ileus	=>cluster: group A	0.1086957	1
TPN, Without familial history, Abdominal distension	=>cluster: group A	0.1086957	1
TPN, Parenteral nutrition, Abdominal distension	=>cluster: group A	0.1086957	1

Figure 1: Clinical Features.

Results

The total number of extracted potential combinations of clinical features was 99,677. By choosing high support value, combinations of high frequency were selected. Eventually, we obtained 32 pattern of group A (support > 0.10), 42 pattern of group B (support > 0.28), 40 pattern of group C (support > 0.13). An example list of raw data on group A was shown in Figure 1. The extracted distinctive features associated with group A were fully dependent on PN (support = 0.120), without familial history (support = 0.120), presence of intestinal dysmotility, intestinal obstruction, and functional ileus (support = 0.120), without mechanical obstruction (support = 0.120), presence of abdominal distension (support = 0.109); associated with group B were require intestinal stoma for decompression (support = 0.337), oral intake of usual diet (support = 0.337), presence of intestinal dysmotility, intestinal obstruction, and functional ileus (support = 0.337), without mechanical obstruction (support = 0.326),

presence of abdominal distension (support = 0.293), no histopathological abnormalities in the intramural ganglion cells (support = 0.293), presence of highly dilated bowel (support = 0.283); associated with group C were no requirement of intestinal stoma for decompression (support = 0.163), oral intake of usual diet (support = 0.163), presence of intestinal dysmotility, intestinal obstruction, and functional ileus (support = 0.163), presence of abnormally dilated bowels on plain abdominal radiograph (support = 0.152), without mechanical obstruction (support = 0.152), presence of highly dilated bowel (support = 0.141), no histopathological abnormalities in the intramural ganglion cells (support = 0.130). The Lift value for each group was more than 1.0 (group A; 6.133, group B; 2.486, and group C; 5.412). Hence the relationships evaluated in our analysis were confirmed to be statistically assured.

Discussion

From a clinical point of view, patients in group A; who fully depended on PN, and patients in group B; who required permanent intestinal decompression were thought to be severe and intractable cases. The proportion of these cases to all the statistical reviewed cases was parallel to our former report [2]. Nine items of clinical features statistically related to these cases were extracted by Association analysis. The combination to choose 9 items from 87 items becomes 87C9 = 513 billion. It was impossible to analyze by conventional statistical technique such as step-wise selection methods. Even if only 0.1 of a second was taken to investigate any one combination pattern, it will take more than 1625 years to check all.

♦ Dependency on PN become gradually greater in the course
♦ Highly dilated bowels present dysmotility
♦ Ileus is present without mechanical obstruction
♦ Present abdominal distension
♦ Requiring stoma for bowel decompression
♦ No histopathological abnormalities in the intramural ganglion cells are seen
♦ Present abnormally dilated bowels on plain abdominal radiograph
PN, Parenteral nutrition

Table 3: Summary of qualified features for diagnostic criteria of CIIP.

Association rules are a more practical approach. They are 'if/then' statements that help to uncover relationships in a large database [4,10]. Mining data with association rules have widely been used in the field of marketing. For an example, "If a customer buys a loaf of bread and jam, then he is also likely to purchase coffee". The goal is to discover a certain group of customer's behavior or buying patterns of some items that are bought together [11]. Recently, association rule mining has been applied to analyze medical data. The knowledge discovered using this method provides useful information for disease management and/or prevention [5-9]. Different from classical statistical methods, data mining described here is not an approach to identify statistical significances but to reveal frequent item sets in a database. Uncovered relationships are useful to hypothesize the trends in a database. Generally, the first certain numbers of combinations with high confidence, support, and lift values from apriori algorithm are selected for investigation [12-14]. On group A, 32 combinations were detected under the condition of confidence = 1. Besides, 98,893 combinations were chosen in group B and 752 combinations were chosen in group C in this condition. So that we selected the lower limit of support value with which the most frequent 32 combinations were included.

According to the association analysis, statistically extracted features of CIIP covering all the severe and intractable cases are summarized in Table 3. These features may be qualified for future diagnostic criteria of CIIP. Here, familial accumulation was only seen in 4 patients within 2 families in our former survey, hence familial history was excluded from the candidate.

Interestingly, a normal full-thickness histopathological finding was extracted as one of the key features in our analysis. Some investigators are attempting to classify the CIPO as neurogenic, myogenic, mesenchymopathic (arising from dysfunction of interstitial cells of Cajal), or unclassifiable or 'idiopathic' [3,15-17]. Although histopathological evaluation is not required for the diagnosis of CIPO, emerging research suggests histopathology may well become essential for elucidating the pathogenesis of 'idiopathic' cases. And it will be a help of developing optimal treatment modalities in the future. As a future proposal of diagnostic criteria on CIIP, histopathological findings may well be included. However, further considerations of technical issues are required. Goulet et al. [18] suggested full-thickness examinations are necessary at different levels of the intestine. Furthermore, the appropriate sample site, amount of each specimen and suitable staining methods need to be defined to clarify the nature of the disease.

Conclusion

Features of CIIP patients, covering all the severe and intractable cases in Japanese children, were extracted from a nationwide survey dataset using a statistical method, association rule mining. In addition of fundamental symptoms of a functional ileus, the proof of absence on histopathological abnormalities, can be used for candidates of diagnostic criteria of CIIP. It is highly significant that normal full-thickness histopathological finding was statistically extracted as one of key features for CIIP in our analysis. Further discussion will be needed on the technical issues of histopathological evaluations, and to establish reliable diagnostic criteria on CIIP.

Conflicts of Interest

The authors declare that they have no conflicts of interest to disclose.

Acknowledgments

This study was supported by a grant 2011-2013 from The Ministry of Health, Labor Sciences Research Grants for Research on intractable disease (H24-Nanchi-Ippan-037) obtained by professor Tomoaki Taguchi. The authors thank the Japanese Society of Pediatric Surgeons; Japanese Society of Pediatric Gastroenterology, Hepatology and Nutrition; Japanese Study Group of Pediatric Constipation; and the 47 pediatric facilities in Japan participated in the former nationwide survey.

References

1. Rudolph CD, Hyman PE, Altschuler SM, Christensen J, Colletti RB, et al. (1997) Diagnosis and treatment of chronic intestinal pseudo-obstruction in children: report of consensus workshop. J Pediatr Gastroenterol Nutr 24: 102-112.

2. Muto M, Matsufuji H, Tomomasa T, Nakajima A, Kawahara H, et al. (2014) Pediatric chronic intestinal pseudo-obstruction is a rare, serious, and intractable disease: a report of a nationwide survey in Japan. J Pediatr Surg 49: 1799-1803.
3. Stanghellini V, Cogliandro RF, De Giorgio R, Barbara G, Morselli-Labate AM, et al. (2005) Natural history of chronic idiopathic intestinal pseudo-obstruction in adults: a single center study. Clin Gastroenterol Hepatol 3: 449-458.
4. Agrawal R, Srikant R (1994) Fast algorithms for mining association rules. Proc 20th Int Conf VLDB: 487-499.
5. Muranaga F, Uto Y, Kumamoto I (2010) Evaluation of a Data Mining Technique for Detection of Adverse Drug Events using a Pharmacoepidemiological Data Warehouse. The 16th JSPE and the 5th ACPE Joint Meeting 16: 54.
6. Lee DG, Ryu KS, Bashir M, Bae JW, Ryu KH (2013) Discovering medical knowledge using association rule mining in young adults with acute myocardial infarction. J Med Syst 37: 9896.
7. Huang Y, Britton J, Hubbard R, Lewis S (2013) Who receives prescriptions for smoking cessation medications? An association rule mining analysis using a large primary care database. Tob Control 22: 274-279.
8. Simon GJ, Schrom J, Castro MR, Li PW, Caraballo PJ (2013) Survival association rule mining towards type 2 diabetes risk assessment. AMIA Annu Symp Proc 2013: 1293-1302.
9. Iltanen K, Kiviharju S, Ao L, Juhola M, Pyykkö I (2013) Clustering and summarising association rules mined from phenotype, genotype and environmental data concerning age-related hearing impairment. Stud Health Technol Inform 192: 452-456.
10. Agrawal R, Imielinski T, Swami A (1993) Mining Association Rules between Sets of Items in Large Databases. CiteSeerX 1993: 207-216.
11. Silverstein C, Brin S, Motwani R (1998) Beyond Market Baskets: Generalizing Association Rules to Dependence Rules. Data Mining and Knowledge Discovery 2: 39-68.
12. Huff MD, Weisman D, Adams J, Li S, Green J, et al. (2014) The frequency of tetracycline resistance genes co-detected with respiratory pathogens: a database mining study uncovering descriptive trends throughout the United States. BMC Infect Dis 14: 460.
13. Huang Y, Lewis S, Britton J (2014) Use of varenicline for smoking cessation treatment in UK primary care: an association rule mining analysis. BMC Public Health 14: 1024.
14. Iqbal Z, Hoessli DC, Qazi WM, Ahmad M, Shakoori AR, et al. (2015) Exploring the Sequence Context of Phosphorylatable Amino Acids: The Contribution of the Upgraded MAPRes Tool. J Cell Biochem 116: 370-379.
15. Lindberg G, Törnblom H, Iwarzon M, Nyberg B, Martin JE, et al. (2009) Full-thickness biopsy findings in chronic intestinal pseudo-obstruction and enteric dysmotility. Gut 58: 1084-1090.
16. Stanghellini V, Cogliandro RF, de Giorgio R, Barbara G, Salvioli B, et al. (2007) Chronic intestinal pseudo-obstruction: manifestations, natural history and management. Neurogastroenterol Motil 19: 440-452.
17. Amiot A, Cazals-Hatem D, Joly F, Lavergne-Slove A, Peuchmaur M, et al. (2009) The role of immunohistochemistry in idiopathic chronic intestinal pseudoobstruction (CIPO): a case-control study. Am J Surg Pathol 33: 749-758.
18. Goulet O, Sauvat F, Jan D (2005) Surgery for pediatric patients with chronic intestinal pseudo-obstruction syndrome. J Pediatr Gastroenterol Nutr 41 Suppl 1: S66-S68.