Ten-year experience in the management of total colonic aganglionosis
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Abstract

Purpose: The aim of this study was to review the 10 years' experience in the management of patients with total colonic aganglionosis (TCA) and follow-up of their health condition.

Methods: Cases of 25 patients with TCA in the Children’s Hospital of Fudan University from 1996 to 2005 were reviewed and analyzed. The confirmed diagnosis was established by an intraoperative frozen-section biopsy of the rectum, colon, appendix, and ileum. The data included in this study accounted for sex, age, signs of presentation, any familiar history of Hirschsprung disease (HD) or associated abnormalities, and ileal involvement. Plain x-ray films, barium enema, and anorectal manometry were provided for evaluation. The results of surgical management were analyzed for weight at definite operation, blood requirement during operation, the total parenteral nutrition duration, and the pre- and postoperative complications of these patients. Follow-up data were collected regarding growth development, stool frequency, stool consistency, fecal soiling, incontinence, enterocolitis, and anal stricture.

Results: Among 25 patients, 8 (32%) females and 17 (68%) males were diagnosed as having TCA. Sixteen patients (64%) were evaluated at the neonatal period, whereas 9 patients (36%) were evaluated after the neonatal period. All 25 patients received at least 1 plain abdominal radiograph or barium enema at the university hospital before operation.

However, there was no specific pathognomonic finding that may provide a definite diagnosis. Nineteen (76%) patients underwent initial laparotomy at our institute and 6 patients (24%) were operated on beforehand at other hospitals. Twenty-three (92%) patients were diagnosed as having TCA and underwent ileostomy, whereas 2 (8%) patients underwent primary pull-through procedure. Eighteen (72%) patients had undergone definite surgery. Pre- and postoperative complications included enterocolitis (44.4%), perianal excoriation (77.7%), electrolyte imbalance (50%), and anastomotic leak (16.6%). Average duration of total parenteral nutrition before operation was 17.77 ± 12.54 days and after operation was 10.27 ± 5.23 days. Mean follow-up time was 27.6 ± 35.39 months. Two patients had 5 to 6 bowel movements per day. Seven had a frequency of stool ranging between 1 and 3 bowel movements per day. Their bowel movements returned to normal about 12 to 18 months after surgery. On follow-up, the height and weight development of the patients was found to be normal.

Conclusions: Gradual progress was observed in all the patients that took part in the study, and all patients had positive results eventually.

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Index words:
Total colonic aganglionosis (TCA); Diagnosis; Treatment

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Total colonic aganglionosis (TCA), with or without involvement of the small intestine, is a severe form of Hirschsprung disease (HD). The incidence of TCA among all forms of HD is between 2% and 14% [1]. Compared to the classic cases of HD, TCA shows more diagnostic problems and is usually associated with higher morbidity and mortality rates [2]. These cases can easily be missed without a high index of suspicion. Therefore, patients require multiple surgeries for subacute intestinal obstruction [3]. The definitive diagnosis of TCA is obtained by performing laparotomy and intraoperative seromuscular biopsies of the rectum, colon, and ileum [4]. Only a few articles have been published in recent years regarding long-term follow-up interviews of patients with TCA [2]. The purpose of this study was to review the TCA cases of the Children’s Hospital of Fudan University that were treated over the last 10 years and to evaluate the preoperative and postoperative complications and follow-up of the patients involved.

1. Materials and methods

This is a retrospective study of 25 cases of patients diagnosed and treated for TCA with ileal involvement, among 831 cases of HD, at the Children’s Hospital of Fudan University from 1996 to 2005. The confirmed diagnosis was established by an intraoperative frozen-section biopsy of the rectum, colon, appendix, and ileum. We reviewed the medical charts from the library of this hospital and analyzed for sex, age, signs of presentation, any familiar history of HD or associated abnormalities, weight at definite operation, ileal involvement in centimeters, findings during definite operation, blood requirement during operation, duration of total parenteral nutrition (TPN), and the pre- and postoperative complications of these patients. Barium enema and plain x-ray films were obtained from the department of radiology. We analyzed the x-ray films mainly on the transition zone or abnormal contractions of the aganglionic segment for signs of intestinal obstruction and presence of microcolon. Follow-up data were collected from the parents. Families were given a detailed questionnaire over telephone regarding growth development, stool frequency, stool consistency, fecal soiling, incontinence, enterocolitis, and anal stricture. Enterocolitis was defined as the presence of abdominal distention, diarrhea, vomiting, and fever.

All data are reported as mean ± SD throughout.

2. Results

Among 25 patients, 8 (32%) female and 17 (68%) male patients were diagnosed as having TCA. All babies were full term except 1 preterm baby with a birth weight of 1.9 kg. Mean birth weight was 3.302 ± 0.67 kg except the preterm baby. None of the patients had a family history of HD or intrauterine infection during their pregnancy period. There were no associated abnormalities with these patients. Sixteen (64%) of the 25 patients initially presented abdominal distention, vomiting, and delay in passing of meconium at the neonatal period. Among them, 3 patients presented with complete intestinal obstruction with ileal perforation at the time of laparotomy. Nine (36%) patients presented with chronic constipation. They had a history of delayed passage of meconium and mild distention of the abdomen. They were treated at a local hospital with suppositories and enemas to pass stool. Clinical signs and symptoms were relieved after treatment. These patients had used suppositories on and off for some time to pass stool.

Among the 25 patients, during laparotomy, 23 were diagnosed as having TCA and underwent ileostomy, whereas 2 underwent primary pull-through procedure. After ileostomy, 7 patients were excluded because of death (2/23) and refusal of treatment (5/23). Therefore, 18 patients with TCA who had undergone definite surgery were included in the postoperative treatment and follow-up review.

2.1. Diagnosis

Among these 25 patients, 16 (64%) patients were evaluated at the neonatal period, whereas 9 (36%) patients were evaluated after the neonatal period. Six (24%) patients had already been operated on for intestinal obstruction before coming to our hospital. Three of these 6 patients had intestinal stenosis, 2 had malrotation, and 1 had short segment HD. Resection and anastomosis of the intestine, Ladd procedure, and Soave procedure for short segment HD were performed. All these cases were failed diagnoses on laparotomy performed at another hospital.

2.2. Radiological features

All 25 patients received at least 1 plain abdominal radiograph (15 patients) or barium enema (13 patients) at our hospital before operation. Plain abdominal radiographs obtained from almost all the patients with TCA showed characteristic signs of dynamic intestinal obstruction with air-fluid levels or gaseous distention of a small intestine loop. In our series, on barium enema, there was no exact transition zone or abnormal contraction of the aganglionic segment. Five (20%) patients had microcolon (2 before ileostomy and 3 after ileostomy) and 7 (28%) patients showed delayed evacuation of barium on x-ray film after 24-hour follow-up of barium enema. However, there was no specific pathognomonic finding on barium enema studies that may provide a definite diagnosis.

2.3. Laparotomy for diagnosis

Nineteen (76%) patients underwent initial laparotomy at our institute. During the laparotomy, 9 (47%) patients had the
distal intestine in spasmodic phase and the portion proximal to the transition zone was dilated, 2 (10.5%) patients had microcolon, and 3 (15.7%) patients had ileal perforation 18, 10, and 25 cm from the ileocecal valve (ICV), respectively. Intraoperative frozen-section biopsy of the rectum, colon, appendix, and ileum was performed to confirm the diagnosis and the length of ileum involvement through the use of acetylcholinesterase. The range of ileum involvement during the laparotomy from frozen-section biopsy was between 15 and 160 cm for 7 cases that were excluded and between 6 and 50 cm from the ICV for the 18 patients who had undergone definitive pull-through operation (Table 1).

2.4. Definite operation

For definite operation, 16 (88.9%) of 18 patients had undergone stage pull-through procedure and 2 (11.1%) patients had undergone primary pull-through procedure. Among them, 12 (66.6%) patients underwent Martin procedure, 4 patients (22.2%) had Ikeda-Soper procedure, 1 patient had Rehbein procedure, and 1 patient had Soave procedure. Soave and Ikeda-Soper techniques were performed for primary pull-through operation. Most of our patients were treated with Martin procedure: side-to-side anastomosis was performed between the aganglionic colon and the pull-through normal ileum by using a linear stapler device up to the peritoneal reflection on the rectum. Suture was applied to the area about 10 to 15 cm above the peritoneal reflection.

The weight of the patients during definite operation was $6.53 \pm 2.031$ kg (range, 2.1-10 kg) and the age at definite operation was $180 \pm 93.601$ days (range, 56-420 days), except 1 neonate who had an operation at 20 days, which was the earliest in our series, and 1 patient who had undergone Soave pull-through at another hospital and underwent ileostomy after the patient’s symptoms were not relieved.

Thirteen of 16 patients who had stage pull-through procedure had their ileostomy closed at the time of definite operation. Another 3 cases underwent ileostomy closing at a later date because these patients had anastomotic leak and redo ileostomy. Blood transfusion was needed for 15 (83.3%) patients during operation. The length of ileum involvement was the same as that during ileostomy for all the patients who underwent definite pull-through. There was no maturation of ganglion cells in the ileum between the time of ileostomy and definite operation in our series.

2.5. Preoperative complications

Eight patients had 1 of more bouts of enterocolitis. Nine had moderate fluid and electrolyte imbalance after ileostomy, with sunken eyes, dry mucous membrane, and reduced urine output, and abdominal skin pinch retracted slowly. Blood gas analysis showed hyponatremia, hypokalemia, and acidosis. Five patients were severely malnourished and had weights below the 10th percentile. All of these 5 patients had increased skinfold and all of them were treated with conservative management. Total parenteral nutrition was needed for 9 (50%) patients before definite operation. Average duration of TPN was $17.77 \pm 12.54$ days (range, 5-44 days). Five patients were on enteral nutrition for a short period.

2.6. Postoperative complications

Postoperative enterocolitis and anal excoriation were common in our study (Table 2). Enterocolitis occurred in

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### Table 1  Age at definite operation, length of ileal involvement from the ICV, and recent follow-up

<table>
<thead>
<tr>
<th>Age at operation</th>
<th>Length of ileal involvement from ileocecal valve (cm)</th>
<th>Follow-up time after pull-through (mo)</th>
<th>Weight (percentile)</th>
<th>Height (percentile)</th>
</tr>
</thead>
<tbody>
<tr>
<td>18 mo</td>
<td>13</td>
<td>×</td>
<td></td>
<td></td>
</tr>
<tr>
<td>15 mo</td>
<td>12</td>
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<tr>
<td>5 mo</td>
<td>50</td>
<td>6</td>
<td>&lt;10</td>
<td>&lt;25</td>
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<tr>
<td>4 mo</td>
<td>8</td>
<td>30</td>
<td>90</td>
<td>90</td>
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<tr>
<td>10 mo</td>
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<tr>
<td>6 mo</td>
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<td>12 mo</td>
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<td>75</td>
<td>90</td>
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<td>6 mo</td>
<td>40</td>
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<td>12</td>
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<td>90</td>
<td>95</td>
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<tr>
<td>11 mo</td>
<td>15</td>
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<tr>
<td>3.5 mo</td>
<td>10</td>
<td>13</td>
<td>75</td>
<td>90</td>
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<td>7 mo</td>
<td>30</td>
<td>36</td>
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<td>5 mo</td>
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<td>33</td>
<td>50</td>
<td>50</td>
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<tr>
<td>4 mo</td>
<td>12</td>
<td>14</td>
<td>75</td>
<td>75</td>
</tr>
</tbody>
</table>

× indicates patient without follow-up.
2.7. Follow-up

Parents of 8 of the 18 patients were followed up by phone, and parents of 2 patients came to the outpatient department. Mean follow-up time was 27.6 ± 35.39 months (range, 6-120 months). Two patients had 3 to 5 bouts of enterocolitis at the last follow-up and were treated conservatively. Seven of 10 patients had frequency of stool ranging between 1 and 3 bowel movements per day and 2 patients had 5 to 6 bowel movements per day. Only 1 had increased frequency of stool more than 10 times per day. This was because he had recently undergone Martin procedure about 6 to 7 months ago. Seven of 10 patients reported that their bowel movements returned to normal about 12 to 18 months after surgery. Among 10 patients, 5 had normal stool consistency, 3 had loose stool, and 2 had pasty stool. In our study, one patient complained of fecal soiling; no one needed anal dilation for stricture. Five patients with ileal involvement of about 12 cm or less had normal development in terms of body height and weight. Of the 5 patients with ileal involvement of more than 20 cm, 2 had heights below the 25th percentile and weights below the 10th and 25th percentile, respectively (Table 2). However, on follow-up, height and weight development of the patients was found normal.

Table 2 Complications of TCA

<table>
<thead>
<tr>
<th>Complications</th>
<th>No. of patients (n = 18)</th>
<th>Percent</th>
</tr>
</thead>
<tbody>
<tr>
<td>Preoperative enterocolitis</td>
<td>8</td>
<td>44.4</td>
</tr>
<tr>
<td>Postoperative enterocolitis</td>
<td>11</td>
<td>61.1</td>
</tr>
<tr>
<td>Malnourished</td>
<td>5</td>
<td>27</td>
</tr>
<tr>
<td>Wound infection</td>
<td>4</td>
<td>22.2</td>
</tr>
<tr>
<td>Perianal excoriation</td>
<td>14</td>
<td>77.7</td>
</tr>
<tr>
<td>Anastamotic leak</td>
<td>3</td>
<td>16.6</td>
</tr>
<tr>
<td>Fluid and electrolyte imbalance</td>
<td></td>
<td></td>
</tr>
<tr>
<td>After ileostomy</td>
<td>9</td>
<td>50</td>
</tr>
<tr>
<td>After definite surgery</td>
<td>6</td>
<td>33.3</td>
</tr>
<tr>
<td>Jaundice</td>
<td>1</td>
<td>5.5</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>2</td>
<td>11</td>
</tr>
<tr>
<td>Convulsion</td>
<td>2</td>
<td>11</td>
</tr>
</tbody>
</table>

11 patients. Almost all of the patients had liquid stool after definite surgery with stool frequency of more than 10 to 20 times per day, and 14 patients had anal excoriation. Four patients had wound infection. Six patients had fluid and electrolyte imbalance. Three patients had anastomotic leak after operation and underwent ileostomy again. Eleven patients needed TPN after operation. Later, all were weaned from TPN. Average TPN duration was 10.27 ± 5.23 days (range, 5-20 days). One patient developed jaundice after TPN. Ten patients were given enteral nutrition for a short period (range, 5-20 days). Seven patients had pneumonia after operation and 2 had convulsions during the postoperative period because of electrolyte imbalance.

3. Discussion

Total colonic aganglionosis, with or without involvement of the small intestine, is a rare form of HD [5]. Twenty-five patients were diagnosed as having TCA and 18 patients underwent definite pull-through operation in the Children’s Hospital of Fudan University during the 10-year period (1996-2005). In our experience, the incidence of this type of aganglionosis is 3%. None of the cases presented aganglionosis confined to the cecum. All the cases were ultra–long form with ileal involvement.

Some reports have stated that the prevalence in boys and girls is nearly equal, whereas some have stated that the boys are much more affected than girls [1,6]. In our series, boys are much more involved than girls, with a boy-girl ratio of 2:1. The literature review indicates that 80% of patients present in the neonatal period, with abdominal distention, constipation or delay in passage of meconium, and bilious vomiting [7]. In our study, 64% of neonates initially presented themselves with the above clinical feature. Among them, 12% of the patients presented with intestinal obstruction with ileal perforation at the time of laparotomy, and 36% of the patients presented with chronic constipation. Although N-Fekete et al [8] have stated that there was a high rate of TCA cases that passed meconium in the first 24 hours of life, it was found that all patients had delayed passage of meconium in our study. None had passed meconium within 24 hours of life. It had been reported that the familial incidence of TCA is higher than that in patients with classical HD [9,10], but there was no related family history of HD and associated anomalies found in our series.

Total colonic aganglionosis accounts for more diagnostic problems. These patients often require multiple surgeries before definite procedure. In our study, 6 patients (24%) had been operated on previously at some other hospital before confirmed diagnosis was reached. Intestinal obstruction and spontaneous perforation of the intestine in neonates is a common condition and caused by various diseases; 3.2% to 4.4% of bowel perforations occur in patients with HD. In TCA, the perforation developed in the aganglionic colon rather than in the terminal ileum proximal to the ganglionic bowel [11]. If there is bowel obstruction with perforation and peritonitis with unknown etiology in a neonate, careful examination to identify the transitional zone is required. If HD is suspected, frozen-section biopsy may be required to exclude the disease. Resection and anastomosis or repair of the bowel perforation alone may cause failure to notice the proper disease. The clinical and radiologic features including delayed evacuation of barium, abnormal contraction of the intestine, and dynamic ileus may strongly suggest the diagnosis, but they are not diagnostic [12]. In our study, 2 cases with contrast enema evaluation raised clinical suspicion for HD. However, on the whole, there were no specific pathognomonic findings on barium enema to profile a definite diagnosis. There is no alternative than to rely on
Ten-year experience in the management of total colonic aganglionosis

Histopathologic confirmation. The total colon and ileum must be detected carefully during laparotomy in children with long segment HD [13]. The diagnosis was established intraoperatively on seromuscular biopsy of the rectum, colon, appendix, and ileum by the technique using acetylcholinesterase in our department. The extension of aganglionosis was determined at the time of ileostomy in 23 of the patients and at the time of primary pull-through in 2 of the patients.

A number of surgical procedures for treating TCA have been reported. Martin modification is the most widely used technique [14]. Most of our patients underwent Martin procedure modified by the use of staplers. We have also performed Ikeda-Soper, Rehbein, and Soave pull-through procedures. Primary pull-through procedure in HD is safe and effective even in neonates, but for TCA there is a lack of well-explained data [15] except for Barbara et al who have reported treating 4 patients [2]. Two of our patients had a primary pull-through performed in the Children’s Hospital of Fudan University; 1 was performed during the neonatal period and 1 at 3 months of age. The postoperative period was uneventful, and both of the patients are reported to be doing well. Some surgeons hold the view that ganglion cells may mature during the growth of the children, which may reduce the length of resection of the ileum, but we found no improvement in the maturity of the ganglion cells between the time of ileostomy and definite pull-through. Although there may be a chance of incorrect leveling of the aganglionic segment in primary pull-through, based on our experience, primary pull-through procedure had fewer problems with electrolyte imbalance and, hence, less chance of malnourishment compared with stage pull-through with ileostomy. Therefore, if the patients’ condition can be evaluated at the neonatal period, primary pull-through operation can be considered. These patients usually present with intestinal obstruction that needs emergency laparotomy, but edematous and dilated proximal bowel may cause difficulties in primary pull-through. Accurate histochemical diagnosis, thorough pre- and postoperative preparation, and the skill of the surgeon are the goals of successful primary pull-through management. Although minimal access surgery in neonates and infants is secure and well tolerated, we have no experience with laparoscopic surgery for TCA [16].

Definite surgery is usually planned at least 6 months after ileostomy. This ensures a period for growth and clinical observation to determine whether the ileum has developed adequate function. Most of our patients were treated with definite surgery approximately 6 to 14 months after ileostomy. In recent years, because of advances in surgical technique, supporting management, and well-equipped intensive care units, we have performed definite surgery a little earlier. It has been clear that decreased length of the aganglionic segment is related to fewer complications and good postoperative results.

To avoid a too extensive and inadequate surgery, initial diverting ileostomy is performed while waiting for histologic results. However, malnourishment and electrolyte imbalance are the major problems after ileostomy. After the third or fourth week of ileostomy, patients have increased frequency of loose stool and may easily develop electrolyte imbalance. Deficiency of immunity power, early oral intake, and inadequate absorption can be the cause of excessive intestinal fluid loss causing electrolyte imbalance and slowly develop protein-energy insufficiency leading to malnutrition. After ileostomy as well as definite surgery, to ensure an appropriate electrolyte level and energy supply and thus avoid early oral food intake, it is necessary to maintain TPN for some time [1,17].

It is found that the amount of time for TPN depends on the age, general condition of the patients, and the length of ileal involvement. After ileostomy, a longer duration of TPN is needed to maintain energy. In our study, the length of resected small bowel was chosen for comparison. Seven patients aged older than 10 months whose general conditions were normal, with short length of ileal involvement (about 10 to 15 cm), did not need any TPN. These patients were on regular oral diet after some days of surgery. Those patients who had ileal involvement of more than 15 cm needed TPN for quite a long time and were later converted to enteral nutrition. One developed jaundice after TPN. Although TPN is an essential part in the treatment of TCA, it should be replaced as soon as possible with enteral nutrition or oral intake to prevent complications.

Enterocolitis is still the most commonly encountered complication of HD with significant morbidity and mortality. Timely identification and early management of this problem may reduce the severity of disease as well as mortality [18]. In our study, the most frequent postoperative complications were enterocolitis and electrolyte imbalance because of the increase in frequency of loose stool, which were successfully treated with conservative management. Anal excoriation was found in most of our patients. Additional ileostomy after Martin procedure was necessary because of anastomotic leak. Martin’s long side-to-side ileorectal anastomosis, contaminated procedure, and malnourishment could be the cause of anastomotic leak and wound infection. While reviewing the medical literature, we found that there are no major differences in long-term follow-up between the various procedures [19]. However, it is difficult to extract conclusions with so little information when Martin procedure was mainly chosen to treat the patients. Overall, it gives the impression that the problem in TCA is not the surgical management of the condition, but rather its prompt diagnosis and the meticulous handling of the complications [8]. It is motivating that there was no problem with anal stricture in our patients. None of our patients required anal dilatation. Two patients had pneumonia after operation and were transferred to the intensive care unit, and 2 patients had convulsion during the postoperative period because of electrolyte imbalance. All were treated successfully. No deaths in our series were recorded.

It is generally reported that bowel function in patients with HD improves gradually with time after surgery [20,21]. The same was also observed in our study. It was seen that the patients had gradual improvement in their bowel function over
time: these patients had loose or pasty stool for about 12 to 18 months after surgery after which the stool consistency returned to normal. The average frequency of bowel movements decreased annually. Only 1 patient in our series had occasional fecal soiling. On follow-up, we found that he was on a restricted diet to avoid soiling. Growth factor is an issue reported in other series. It seems that the patients with less ileal involvement had normal development and those with extended ileal involvement needed TPN as supplementation. On the whole, the patients with ileal involvement less than 50 cm have normal growth despite complications. This is because of the supportive supplementary treatment and also because the bowel frequency starts to decrease a year after the operation.

4. Conclusion

Only a small proportion of all HD cases is composed of TCA. Although the clinical and radiologic features can be useful in the diagnosis, they are not pathognomonic, and one eventually has to depend on histopathologic evaluation during laparotomy for confirming the diagnosis and the length of involvement. Although there are many pre- and postoperative complications, gradual progress is noted, and most patients have a good outcome over time, although morbidity remains high. In recent times, improvements in supportive care, early detection, and proper treatment have led to the increased rate of survival in TCA.

References