Do Prognostic Factors Exist for Total Colonic Aganglionosis With Ileal Involvement?

By V. Fouquet, P. De Lagausie, C. Faure, J. Bloch, S. Malbezim, L. Ferkhadji, C. Bauman, and Y. Aigrain

Paris, France

Background/Purpose: Total colonic aganglionosis with ileal involvement is estimated at 1 case in 50,000 living births. This pathology has a very variable prognosis, and patients often need long-term parenteral nutrition. The aim of this study is to define prognostic factors for this disease.

Methods: This is a retrospective study from 1980 to 1999, based on 26 cases of total colonic aganglionosis with ileal involvement. The authors analyzed birth term, sex, birth weight, ileal involvement in centimeters, delay to correct level enterostomy, the total parenteral nutrition duration, and the need for constant rate nutritional assistance. The authors studied the following items: Weight, height, complications, clinical state, and nutritional issues. The statistic test is: LOG RANK (analysis of censured datas and comparison of survival diagram).

Results: The only prognostic factor is the length of ileal involvement. All the children with ileal involvement less than 50 cm, except for 2, did not need long-term nutritional assistance; for those with ileal resection over 50 cm, long-term nutritional assistance was needed. Total colonic aganglionosis is a very serious illness (2 children had a small bowel transplantation, and 2 are waiting for one). The prognosis is even worse when associated with a polymalformation syndrome (50% of the children died).

Conclusion: The major prognostic factor is the length of small bowel not involved in the total colonic aganglionosis.

INDEX WORDS: Total colonic aganglionosis, Hirschsprung’s disease, parenteral nutrition, short small bowel.

TOTAL COLONIC AGANGLIONOSIS (TCA) represents about 10% of all cases of Hirschsprung’s disease. It is one of the most common causes of neonatal intestinal obstruction. It occurs approximately once in every 50,000 births. The diagnosis is based on acetylcholinesterase activity in colic and ileal biopsies. The illness can affect the small bowel over a few centimeters from the ileocecal valve, or it also can concern the small bowel in its totality. Children suffering from this disease often need long-term total parenteral nutrition (TPN), which will determine morbidity and mortality. Our objective is to define prognostic factors of life expectancy for children presenting with this pathology.

MATERIALS AND METHODS

This is a retrospective study from 1980 to 1999. The charts of 26 cases of TCA treated at the ROBERT DEBRE hospital in Paris were reviewed. We analysed length of gestation, birth weight, sex, age, initial presentation, associated abnormalities, delay between first symptom and enterostomy at the correct level, ileal involvement in centimeters, delay between enterostomy and pull-through procedure, type of pull-through procedure, duration of total parenteral nutrition (TPN), the possibility of weaning of nutritional assistance (NA), growth and height, number of abdominal operations, and hereditary factors, as well as searching for the RET gene.

Impact of the studied parameters on thriving, complications, clinical state, and type of nutritional support was analyzed with LOG RANK (analysis of censured data comparison of survival diagram).

RESULTS

We reviewed the charts of 26 children aged 4 months to 19 years in March 1999. Average gestational age was 39.2 weeks (range, 35 to 42 weeks); 6 children were premature. Mean birth weight was 3,210 g (range, 1,650 to 4,200 g). Among them, 3 children were under 2,500 g. There were 16 girls (61.5%) and 10 boys (38.5%); the sex ratio was 1:6. The overall survival rate was 84.7% (22 of 26 patients), 2 children underwent a bowel transplantation, and 2 are awaiting transplantation. Seven children still have NA (4 with TPN, 3 with enteral nutrition [average duration 3 years]).

Eight children (30.5%) had associated abnormalities: 1 atresia of the small bowel, 1 Down’s syndrome, 1 On-dine’s syndrome, 1 Glasgow’s syndrome (died), 2 Shaah Waardenburg’s syndrome (2 died), 1 unilateral kidney agenesis, and 1 amniotic sequence.
Age of first symptoms varied from 0 to 15 days (average, 7 days); the 4 deaths had early diagnosis (1 to 2 days). Three children had initial presentation at more than 10 days, 2 of them are well and are weaned from NA, the last one is still under NA.

The disease always presented as an intestinal obstruction. Six patients suffered from a deterioration of their general condition; none of them had enterocolitis. One child presented with an acute intussusception. Seven children had normal meconial elimination within 24 hours of life, and 15 evacuated meconium after an additional 24 hours. We have no information on 4 cases.

The delay between first symptoms and enterostomy at the correct level was 1 day to 3.5 years (average, 5 months = 149 days). In 69.2% of the cases, the delay was less than 1 month, between 1 month and 1 year in 19.2%, and over 1 year in 11.6%. Ten children underwent fecal diversion in a pathologic area for 10 days to 3.5 years (average duration, 11.3 months). Among these 10 children, 4 were weaned from TPN (average duration is 9.1 months), 2 died (average 6 months), 1 underwent transplant (1.2 years), 2 are awaiting transplantation (average, 26 months), and 1 still has TPN (15 days). For children still in NA (7 of 26), the average delay before enterostomy was 265 days (4 of 7 had a late enterostomy at the correct level). The LOG RANK test comparing the duration of enterostomy at the correct level and the total duration of TPN did not show any significant difference ($P = .512$).

Involved segment of small bowel extended from 1 cm to more than 1 m from ileocecal valve (average, 49.3 cm). Of the 7 children still having NA and the 4 deaths (11 children), only 2 had resection smaller than 50 cm, the others had resection greater than 50 cm (average, 94.3 cm; Fig 1).

In the 15 children weaned from their NA, the ileal involvement was smaller than 50 cm (average, 16.2 cm).

We only know the length of remaining small bowel, when the length of resected small bowel was above 50 cm. For the 4 children who died, this length was, respectively, 15 cm, 15 cm, 37 cm, and 135 cm. For the children still on NA, this length was, respectively, 20 cm, 37 cm, 60 cm, 90 cm, and 95 cm. Eighteen patients (69.2%) ultimately had a definitive procedure using the Duhamel pull-through technique (one case was done laparoscopically); 2 children needed a new ileostomy 2 years and 3 years after the procedure, respectively; and 6 patients are still in enterostomy. There were 2 early deaths before intestinal diversion, and 2 late deaths before definitive procedure (1 at 3 years, and 1 at 5 years).

The delay between enterostomy and the pull-through varied from 5 months to 5.5 years (average, 2 years and 3 months). In 45%, this delay was under 18 months.

The duration of TPN was between 0 and 74 months, (average, 20.2 months) most often only before the pull-through procedure (15 of 18 children). It is worthwhile noting that 3 children never had TPN (all had a resection inferior to 10 cm; Fig 2).

The Log Rank test comparing the ileal involvement in centimeters and the duration of TPN shows a significant difference between the population of patients who had a resection inferior to 50 cm (9.7 months of TPN) or superior (70.2 months of TPN) to 50 cm (mean difference, 60 months; $P = .000254$; Fig 3).

Continence was looked for in 15 children: 6 were continent before 5 years, 5 were continent between 5 and 9 years, and one was incontinent after 9 years; 10 still have a stoma or died, 1 is to young to be continent, and we have no information for the last 3. All children had at least one complication and underwent between 1 and 9 surgical interventions. Complications were water and electrolyte decompensation (average, 9 episodes per child), septicemia (average, 7 episodes per child), stoma prolapse (average, 4 episodes per child) and thoracic ganglioneuroma ($n = 2$); a new resection of spur was
needed for 2 of the 18 children after Duhamel pull-through. One child had a spur ulceration.

We studied the growth and thriving status. The weight varied from $-2.5$ SD to $+2.5$ SD (average, 0), height from $-4$ SD to $+2$ SD (average, $-0.7$ SD). When comparing the thriving of children weaned from TPN and those still on TPN we found no significant difference (Fig 4).

Three patients had a familial history of aganglionosis (11.1%). We did not find the RET oncogene in 15 children.

**DISCUSSION**

Total colonic aganglionosis with ileal involvement (TCAWII) represents a severe disease. In reviewing the medical literature we found that the mortality rate fluctuates from 8% to 30%.1-4 The prognosis is worsened when TCAWII was associated with other malformations.

Our series confirms the finding of the literature in that term, birth weight, and sex are not prognostic factors.1-3 Boys are much more involved than girls, although we found the opposite in our study. The overall survival rate is 84.7%.5,6: 75% for the girls and 100% for the boys. Our impression is that although sex was not a statistically significant prognostic factor, boys seemed to do less well than girls. This is not similar to rates reported in other series.1,4 In our series, intestinal occlusion was the main presentation; the diagnosis was established by biopsy and acetylcholinesterase coloration. The meconium evacuation was late for 68% of patients. It can be a good sign for diagnosis (sensitivity is 68%).3,7

The enterostomy at the correct level is sometimes delayed by colostomy or an ileostomy at an incorrect level done in the first place (10 children), this is because of the difficulty in identifying histologically the normal small bowel plexus. This is the reason some children who have stomas in the pathologic area arrived in our surgical departement. Failure to thrive and new occlusive
syndromes lead to new biopsies and permitted to choose the ideal ileal level for stoma. There was no significant difference in terms of septic complications, growth, and TPN duration between those who had the first stoma at the pathologic level and those who did not. We think that the pathogenesis of the ileal dysmotility (post obstructive enteropathy lesion), found in almost all cases of TCA, is more likely congenital than the consequence of the distension.

The length of resection is the main prognostic factor for TPN duration, survival rate, and clinical result.

Ileal resection inferior to 50 cm is a very good prognostic factor. If the resection is over 120 cm (6 children), the prognosis is worse, with a 50% mortality rate (3 of 6). Sixteen percent underwent transplant (1 of 6), and 34% are awaiting transplantation (2 of 6). The 2 children who required a new ileostomy had their Duhamel procedure at 9½ months and 3½ years, respectively. We chose to compare the length of the resected small bowel instead of length of the remaining small bowel because we had this information for all the patients. With the information about the length of remaining small bowel, we can observe for patients who died, this length was in 75% of the cases, inferior to 50 cm, and for the patient still on NA, each time the length of resected small bowel is more than 50 cm, then the remaining small bowel is less than 100 cm. However, it is impossible to draw conclusions with so little information.

The duration of TPN is directly related to small bowel involvement length. When the resection was inferior to 50 cm, the average duration of the TPN was 9.7 months, and when the resection was superior to 50 cm, the average duration was 70.2 months. There are several possible explanations for these results: (1) A congenital or a postobstructive dysmotility probably exists independently from the presence of the plexus, and it deeply disturbs the small bowel. (2) We have more children with high ileal involvement than the other series. (2 of the deceased children had a severe short bowel). (3) The number of associated syndromes was more important than in other reported series and has a worse prognosis (2 deceased children had a Shaa Waadenburg’s syndrome). (4) In short bowel syndrome, children will need TPN on a long-term basis. Stopping nutritional assistance is almost impossible. Definitive treatment is small bowel transplantation (2 patients already undergone transplant and 2 others on the waiting list).

We found that the main growth failure in these children concerned their height curve with more or less normal weight curves. This is in controversy with others series reported in the literature. Growth failure is not correlated with the length of remaining small bowel. In fact, with exclusive TPN, growth can be adequately corrected. For the other complications (septicemia, water, and electrolyte decompensation), the only prognostic factor is the length of the small bowel involvement (over 120 cm the children died, received graft, or are waiting for transplantation). The complications are enhanced by associated syndromes and by TPN duration. The definitive repair always was done with a Duhamel pull-through procedure after weaning from TPN. One intervention was assisted laparoscopically. We have no experience with the right colon patch or the other methods of pull-through procedure. Surgery was indicated for those children who were clinically stable and mostly off TPN. After surgical treatment, most of them were weaned of TPN (15 of 18). Two of them needed a new ileostomy. The surgery timing often does not seem to influence this bad evolution. The use of Duhamel pull-through procedure on the small bowel has a late positive effect on continence even in total colonic aganglionosis cases.

Genetic studies also have been of great interest; in our series, the hereditary factors represent about 10% (3 patients), much closer to the 10% to 20% found in the literature. One of the 3 is doing well and weaned from NA, one died, and the last one is sick. Although the hereditary factor seems a poor prognostic factor, our series is too small to conclude. More than half of the patients underwent a search for anomalies of the RET gene, and none was positive.

Except the TCAWII associated with polymalformation syndromes (50% of the children died), the major prognostic factor is the length of the small bowel involvement. Children with small bowel involvement less than 50 cm had good results, shorter TPN, and pull-through before 18 months. With small bowel involvement more than 50 cm, it is very difficult to stop the NA, with short bowel, we often had to perform a bowel transplantation (2 children received graft, and 2 are waiting for transplantation).

REFERENCES

5. Ikeda K, Godo S: Total colonic aganglionosis with or without