Total Colonic Aganglionosis: Reappraisal of Contrast Enema Study

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ABSTRACT

Total colonic aganglionosis (TCA) is a rare form of Hirschsprung disease (HD). It is difficult to be diagnosed on contrast enema because the radiographic findings are variable. The study aims to re-evaluate the contrast enema findings of TCA. From 2001 to 2009, 14 patients (11 males, 3 females; ages from 1 day to 6 months) with pathologically proven TCA were reviewed for demographic features, clinical presentations, pathology reports, radiographic and contrast enema findings. In addition, the radiographic and contrast enema findings of 53 patients with non-TCA HD were reviewed and compared with those of TCA. Among the imaging findings, a short and rigid colon, small bowel dilatation, microcolon, and radiographic transition zone proximal to the cecum were statistically more significant in patients with TCA than in patients with non-TCA HD \(P < 0.001\). In conclusion, TCA is a colon disease presenting as small bowel obstruction clinically and radiographically. Although the radiographic findings of TCA are variable, TCA could be suspected when the initial radiograph shows small bowel dilatation and contrast enema shows a short and rigid colon, radiographic transition zone proximal to the cecum, poor rectal distensibility, colonic wall irregularity and delayed contrast emptying. In addition, biopsy should be performed to make a definite diagnosis. According to the caliber of the colon on contrast enema, a subgrouping approach may be useful in the differential diagnosis and be helpful in early diagnosis and exclusion of TCA.

Hirschsprung disease (HD) is a developmental disorder of the enteric nervous system which is characterized by the absence of ganglion cells in the myenteric and submucosal plexuses of the distal intestine [1]. The arrest of craniocaudal migration of the ganglion cells from the neural crest is thought to be the etiology of HD [2]. Spasm, chronic contraction and poor coordinated peristalsis of the aganglionic distal bowel lead to the functional intestinal obstruction which is the characteristic presentation of HD. Children with HD typically present in the neonatal period with abdominal distention, feeding intolerance, bilious vomiting and delayed passage of meconium. Some patients who do not present with obvious clinical symptoms in the neonatal period could present with chronic constipation when they get older. Other patients could present with enterocolitis which is characterized by fever, abdominal distention and diarrhea [1]. In the majority of HD (67% to 79%), the transition zone between the ganglionic and aganglionic bowel is in the rectosigmoid colon [3, 4]. Total colonic aganglionosis (TCA) is defined as aganglionosis of the entire colon with or without extension into the small intestine, which accounts for 3% to 12% of HD [3-8].

Full-thickness biopsy of the colon in the operation is the gold standard for the diagnosis of HD. For the
contrast enema is a potential treatment and examination of enterocolitis. Compared with barium enema, water-soluble contrast medium in neonates and patients with TCA. One patient with TCA was excluded because contrast enema was not performed. The medical records of the 14 patients with TCA and the 53 patients with non-TCA HD were reviewed in consensus by two pediatric radiologists: one with 15 years of experience (C.-J. W.) and one with 10 years of experience (W.-C. L.). Seven imaging findings were assessed: small bowel dilatation, microcolon, a short and rigid colon, poor rectal distensibility, colonic wall irregularity, radiographic transition zone, and delayed contrast emptying.

There were some terms to be defined in the following. First, the caliber of the colon was further classified into microcolon (Fig. 1a) and non-microcolon (Fig. 1b). Microcolon was defined as a colon caliber which was generally less than the interpedicular space of the L1 vertebra. The normal caliber colon or dilated colon was classified into the subgroup of non-microcolon. Second, a short and rigid colon was defined as the loss of redundancy of the sigmoid colon with rounding of the splenic and hepatic flexures. Sometimes, it could appear as a question mark-shaped colon (Fig. 1c). Third, poor rectal distensibility was defined as a persistent poor distention of the rectum (Fig. 1d). Fourth, colonic wall irregularity was defined as a serrated contour of the colon (Fig. 1e). Fifth, the radiographic transition zone was the location of obvious caliber change in the bowel (Fig. 1f). Sixth, delayed contrast emptying was defined as retained contrast medium proximal to the sigmoid colon on a radiograph which was obtained from 24 to 48 hours after the contrast enema.

**Statistical analysis**

The Fisher’s exact test was used to compare the imaging findings of the two patient groups, those with TCA and those with non-TCA HD. A P value of less than 0.05 was considered to indicate a statistically significant difference.

**RESULTS**

Demographic features, pathology reports, and imaging findings of the patients with TCA are shown in Table 1. Comparison of imaging findings of TCA and non-TCA HD are shown in Table 2.

**Demographic, clinical, pathologic data of TCA**

The patients were predominantly males (11 males, 3 females, male-to-female ratio = 4:1) and full-term (12/14). The ages at the time of contrast enema ranged from 1 day to 6 months, and were usually during the neonatal period (10/14). The clinical presentations included vomiting (14/14), abdominal distention (13/14), feeding intolerance (4/14),
delayed passage of meconium (3/14), enterocolitis (2/14), and bowel perforation (2/14). Almost all the patients had aganglionic segments extending to the cecum or the distal ileum, and just one (case 7) had an aganglionic segment extending to the proximal ileum (100 cm proximal to the ileocecal valve). One patient (case 2) had the simultaneous occurrence of TCA with ileal atresia. There was no related family history found in patients with TCA.

**Imaging findings**

Among the imaging findings assessed in our study, a short and rigid colon, small bowel dilatation, microcolon, and radiographic transition zone proximal to the cecum were statistically more significant in patients with TCA than in patients with non-TCA HD ($P < 0.001$). A short and rigid colon was noted in 14 of 14 patients with TCA (100%) while in one of 53 patients with non-TCA HD (1.9%). Small bowel dilatation was noted in 14 of 14 patients with TCA (100%) while in one of 53 patients with non-TCA HD (1.9%). The contrast enema showed microcolon in three of 14 patients with TCA (21.4%) while in one of 53 patients with non-TCA HD (1.9%). The radiographic transition zone of the 14 patients with TCA was noted at the region from the distal descending colon to the proximal ascending colon in one (7.1%) and at the region proximal to the cecum in 13 (92.9%). For the 53 patients with non-TCA HD, the radiographic transition zone was noted at the region from the anus to the proximal sigmoid colon in 43 (81.1%), at the region from the distal descending colon to the proximal ascending colon in four (7.5%), at the region proximal to the cecum in one (1.9%) and there was no discernible radiographic transition zone in five (9.4%).

There were no statistically significant differences in the presence of poor rectal distensibility, colonic wall irregularity, and delayed contrast emptying between patients with TCA and non-TCA HD. The poor rectal distensibility

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**Figure 1**

1a 1b 1c 1d 1e 1f

Figure 1. a. Microcolon, case 7. b. Non-microcolon, case 8. c. Short and rigid colon with a “question mark” appearance, case 3. d. Poor rectal distensibility (arrow), case 1. e. Colonic wall irregularity (arrow), case 5. f. Radiographic transition zone at the terminal ileum (arrows), case 3.
<table>
<thead>
<tr>
<th>No.</th>
<th>Age at enema (days)/ Gender</th>
<th>Gestation</th>
<th>Imaging findings</th>
<th>Pathologic transition zone</th>
<th>Remarks</th>
</tr>
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<tr>
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<td>Small bowel dilatation</td>
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<td>14</td>
<td>69/M Preterm</td>
<td></td>
<td>✓</td>
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</table>

N/A: not available; TCA: total colonic aganglionosis
was noted in 10 of 14 patients with TCA (71.4%) while in 45 of 53 patients with non-TCA HD (84.9%). The colonic wall irregularity was noted in eight of 14 patients with TCA (57.1%) while in 10 of 53 patients with non-TCA HD (18.9%). Ten of 14 patients with TCA and 32 of 53 patients with non-TCA HD had available 24 to 48 hours post-evacuation radiographs for review. Delayed contrast emptying on 24 to 48 hours post-evacuation radiograph was noted in six of 10 patients with TCA (60%) while in 15 of 32 patients with non-TCA HD (46.9%).

DISCUSSION

In the following paragraphs, we will review the demographic and clinical features of TCA. In addition, we will discuss the imaging findings and the differential diagnosis of TCA.

Hirschsprung disease is a male predominance with the male-to-female ratio of 3:1 to 4:1 [4, 8, 20]. Previous study stated the longer the extent of aganglionosis, the smaller ratio of male-to-female [3]. The male-to-female ratio of TCA was reported from 1:1 to 6:1 [8, 18, 21-23], and the ratio is 4:1 in our study. Most of our patients with TCA presented in the neonatal period (71%). The results of our study group are consistent with the previous studies [21, 23]. Some studies reported that the presentation of TCA might be much later than expected and 14% of TCA present after the age of six months [24]. In addition, there are few case reports of TCA presenting as late as adolescence and early adulthood [25-27]. In our study, the oldest patient with TCA presented at the age of six months.

The clinical presentations of TCA are similar to those of classic cases of HD. In our study, most of the patients presented with symptoms of neonatal bowel obstruction such as delayed passage of meconium, abdominal distention, feeding intolerance and bilious vomiting. Few patients presented with chronic constipation and enterocolitis. Although it is rare, bowel perforation is one of the possible clinical manifestations and potential complications when performing contrast enema on these patients. In the literature, bowel perforation was noted in 3% to 4% of patients with HD [6, 28]. Most of them were long segment HD or TCA [28]. In our study, two patients (14.3%) developed bowel perforation—one presented in the initial presentation (case 2) and the other had the attack during the contrast enema (case 6).

It was reported that the incidence of a positive family history in TCA is higher than that in other forms of HD [8], but in our study there was no related family history found.

Table 2. Comparison of imaging findings of TCA and non-TCA HD

<table>
<thead>
<tr>
<th>Imaging findings</th>
<th>TCA (n=14)</th>
<th>Non-TCA HD (n=53)</th>
<th>P Value</th>
</tr>
</thead>
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<tr>
<td>Small bowel dilatation</td>
<td>14 (100)</td>
<td>1 (1.9)</td>
<td>&lt;0.001</td>
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<tr>
<td>Microcolon</td>
<td>3 (21.4)</td>
<td>1 (1.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Short and rigid colon</td>
<td>14 (100)</td>
<td>1 (1.9)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Poor rectal distensibility</td>
<td>10 (71.4)</td>
<td>45 (84.9)</td>
<td>0.257</td>
</tr>
<tr>
<td>Colonic wall irregularity</td>
<td>8 (57.1)</td>
<td>10 (18.9)</td>
<td>0.082</td>
</tr>
<tr>
<td>Delayed contrast emptying</td>
<td>6 (60) b</td>
<td>15 (46.9) c</td>
<td>1</td>
</tr>
<tr>
<td>Radiographic transition zone</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No transition zone</td>
<td>0 (0)</td>
<td>5 (9.4)</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Zone 1 d</td>
<td>0 (0)</td>
<td>43 (81.1)</td>
<td></td>
</tr>
<tr>
<td>Zone 2 d</td>
<td>1 (7.1)</td>
<td>4 (7.5)</td>
<td></td>
</tr>
<tr>
<td>Zone 3 d</td>
<td>13 (92.9)</td>
<td>1 (1.9)</td>
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</tr>
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</table>

a One case in the group of non-TCA HD is skip segment HD with aganglionosis involving the rectosigmoid colon and the terminal ileum. The patient presented with a short and rigid colon, small bowel dilatation, microcolon, poor rectal distensibility and delayed contrast emptying on the radiograph and contrast enema imaging.

b 10 of 14 patients with TCA had available 24 to 48 hours post-evacuation radiographs. Delayed contrast emptying on 24 to 48 hours post-evacuation radiograph was noted in 6 of 10 patients.

c 32 of 53 patients with non-TCA HD have available 24 to 48 hours post-evacuation radiographs. Delayed contrast emptying on 24 to 48 hours post-evacuation radiograph was noted in 15 of 32 patients.

d Zone 1: from the anus to the proximal sigmoid colon; Zone 2: from the distal descending colon to the proximal ascending colon; Zone 3: proximal to the cecum

HD: Hirschsprung disease; TCA: total colonic aganglionosis
in patients with TCA. TCA may be associated with a wide range of other anomalies such as congenital heart disease, malrotation, intestinal atresia, Down’s syndrome, mental retardation, cleft lip and palate [8]. In our study, one patient with TCA had ileal atresia. The simultaneous occurrence of TCA with intestinal atresia is rare. There are only a few case reports in the literature [29, 30].

As compared to the classic HD, TCA is associated with higher morbidity and mortality rates [4, 5, 8]. Enterocolitis is the most commonly encountered complication with significant morbidity and mortality [5, 31]. The incidence of enterocolitis was suggested to increase in patients with delayed diagnosis [32, 33]. It highlights the importance of early diagnosis of TCA.

The surgical management of HD has progressed from a two- or three-stage approach to a one-stage and minimal access procedure. The treatment of TCA was modified from the procedures used for classic cases of HD. The choice of the surgical procedure is partly based on the anticipated level of transition zone on contrast enema. The preoperative knowledge of the extent of aganglionic bowel can greatly influence the surgical planning [11-13]. In addition, it might reduce the operative time and potentially prevent an incorrect determination of transition zone in the operation [14]. Thus, the findings on contrast enema which might raise the suspicion of TCA are important.

In the literature review, there is a wide spectrum of radiographic features of TCA on contrast enema and the diagnosis of TCA is therefore usually difficult to be established [14-18]. There were some retrospective studies of TCA focusing on the imaging findings [14, 17, 18]. However, development in the radiographic diagnostic techniques of TCA has seldom occurred.

In our cases, all patients with TCA showed dilated small bowel loops on the initial abdominal plain radiographs which indicate small bowel obstruction. In contrast, small bowel dilatation was rarely seen in patients with non-TCA HD except for one case of skip segment HD. This case presented with small bowel dilatation due to one segment of aganglisis involving the terminal ileum.

The radiographic transition zone has been reported to be the most reliable imaging finding of HD [34, 35]. But it had been documented to be unreliable in TCA [12-14]. In our study, 13 patients with TCA (92.9%) had radiographic transition zones at the ileum, which were consistent in the pathological transition zones. Only one patient (Fig. 2, case 9) had a radiographic pseudo-transition zone at the transverse colon. Based on the results and experiences, the radiographic transition zone is not unreliable in TCA. In fact, the reason why it is considered to be unreliable is because it might be difficult to be well evaluated. The location of the transition zone in TCA is usually at the terminal ileum and
Imaging of total colonic aganglionosis

Colonic wall irregularity was thought to result from denervation hypersensitivity of smooth muscle or association with colitis [34]. In the literature review, colonic wall irregularity has been reported to have low sensitivity and high specificity in HD [10]. In our study, this imaging finding was noted in 57.1% of patients with TCA and in 18.9% of patients of non-TCA HD. It might be helpful for diagnosis of TCA.

Delayed contrast emptying was defined as retained contrast medium proximal to the sigmoid colon on the radiograph which was obtained from 24 to 48 hours after contrast enema. In the literature review, it has been reported to be a imaging finding of HD with poor specificity [10, 34, 35]. Delayed contrast emptying might be helpful to differentiate TCA from meconium plug syndrome [34]. Meconium plug syndrome could be treated by contrast enema, and it shows good evacuations of contrast medium on the delayed films. The imaging features discussed above might be helpful to distinguish TCA from other diseases with similar radiographic findings. According to the caliber of colon on contrast enema, we divide the imaging findings of TCA into two subgroups—microcolon and non-microcolon to make differential diagnosis more systemic. The common differential diagnosis of the two subgroups was discussed in the following paragraphs and summarized in Fig. 3.

The differential diagnosis of microcolon includes small bowel atresia, meconium ileus, TCA and other causes of small bowel obstruction such as adhesion band and post-necrotizing enterocolitis stricture. Small bowel atresia should be suspected if there is no contrast medium to be further refluxed into the dilated small intestine. Meconium ileus should be considered when seeing a dilated distal ileum with refluxed contrast which containing many round or ovoid filling defects. Besides microcolon, TCA should have other

Figure 3

Figure 3. Subgrouping approach in the imaging analysis of TCA. HD: Hirschsprung disease; TCA: total colonic aganglionosis; NEC: necrotizing enterocolitis
abnormal findings such as a short and rigid colon, radiographic transition zone proximal to the cecum, poor rectal distensibility, colonic wall irregularity and delayed contrast emptying, which we have discussed above. Adhesion band and post-necrotizing enterocolitis stricture may also result in microcolon, but they are considered in the differential diagnosis only if the patient has related clinical history.

The differential diagnosis of non-microcolon in patients with distal intestinal obstruction includes meconium plug syndrome, long segment HD and TCA. Meconium plug syndrome which is an entity in the spectrum of functional neonatal intestinal obstruction [39] has clinical symptoms and radiographic features of distal intestinal obstruction. The symptoms of distal intestinal obstruction in meconium plug syndrome could be relieved after water-soluble contrast enema [1]. In addition, there is usually no retained contrast medium in the colon on the 24 to 48 hours delayed radiograph [34]. Long segment HD is very difficult to distinguish from TCA by contrast enema. Due to the same etiology and similar extent of involvement, the radiographic features of TCA such as a short and rigid colon, poor rectal distensibility, colonic wall irregularity and delayed contrast emptying could also be presented in patients with long segment HD. The major difference between long segment HD and TCA is the location of transition zone. In TCA, the transition zone locates at the cecum or small intestine. However, the pseudo-transition zone could be presented in patients with TCA like the case in our study (Fig. 2, case 9). It could make us confused TCA with long segment HD.

The imaging findings of patients with non-TCA HD were reviewed and compared with those of TCA. Among the imaging findings, a short and rigid colon, small bowel dilatation, microcolon, and radiographic transition zone proximal to the cecum were statistically more significant in patients with TCA than in patients with non-TCA HD (P < 0.001). It is reasonable that most of the cases with non-TCA HD are short segment HD. The aganglionicosis involves short segment distal colon, which seldom result in a short and rigid colon, small bowel dilatation, microcolon, and radiographic transition zone proximal to the cecum.

In conclusion, TCA is a colon disease presenting as small bowel obstruction clinically and radiographically. Although the radiographic findings of TCA are variable, they can be divided into two subgroups. In the subgroup of microcolon, TCA should be differentiated from small bowel atresia, meconium ileus, adhesion band and post-necrotizing enterocolitis stricture. In the subgroup of non-microcolon, TCA should be differentiated from meconium plug syndrome and long segment HD. We need to take TCA into consideration when the initial radiograph shows small bowel dilatation and contrast enema shows a short and rigid colon, radiographic transition zone proximal to the cecum, poor rectal distensibility, colonic wall irregularity and delayed contrast emptying. In addition, biopsy should be performed to make a definite diagnosis.

REFERENCES
